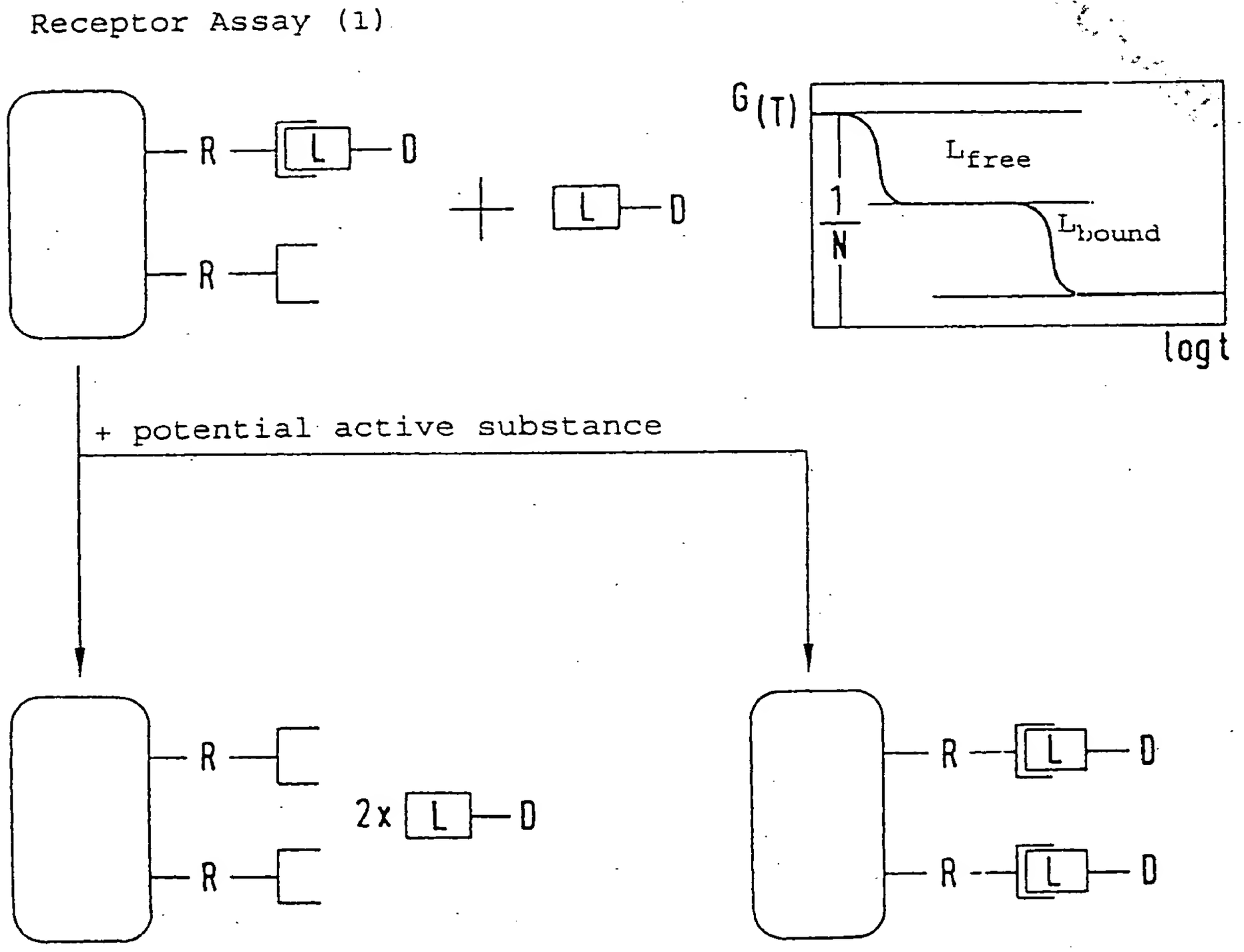
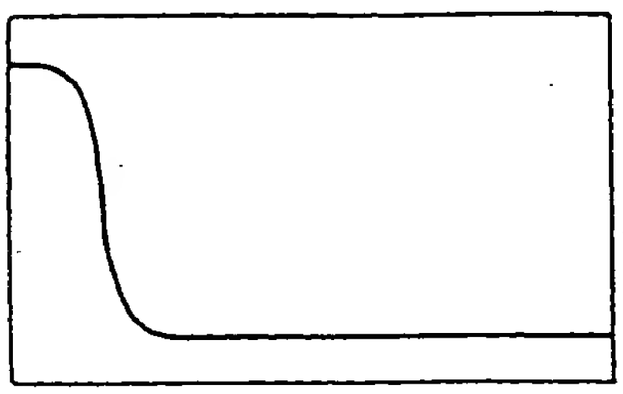
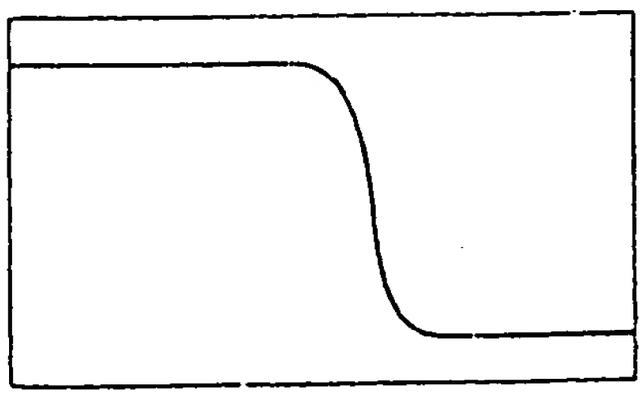
FIG. 1





- antagonistic activator
- antagonistic blocker
- allosteric blocker



- allosteric complex stabilizer (blocker or activator)

FIG. 2

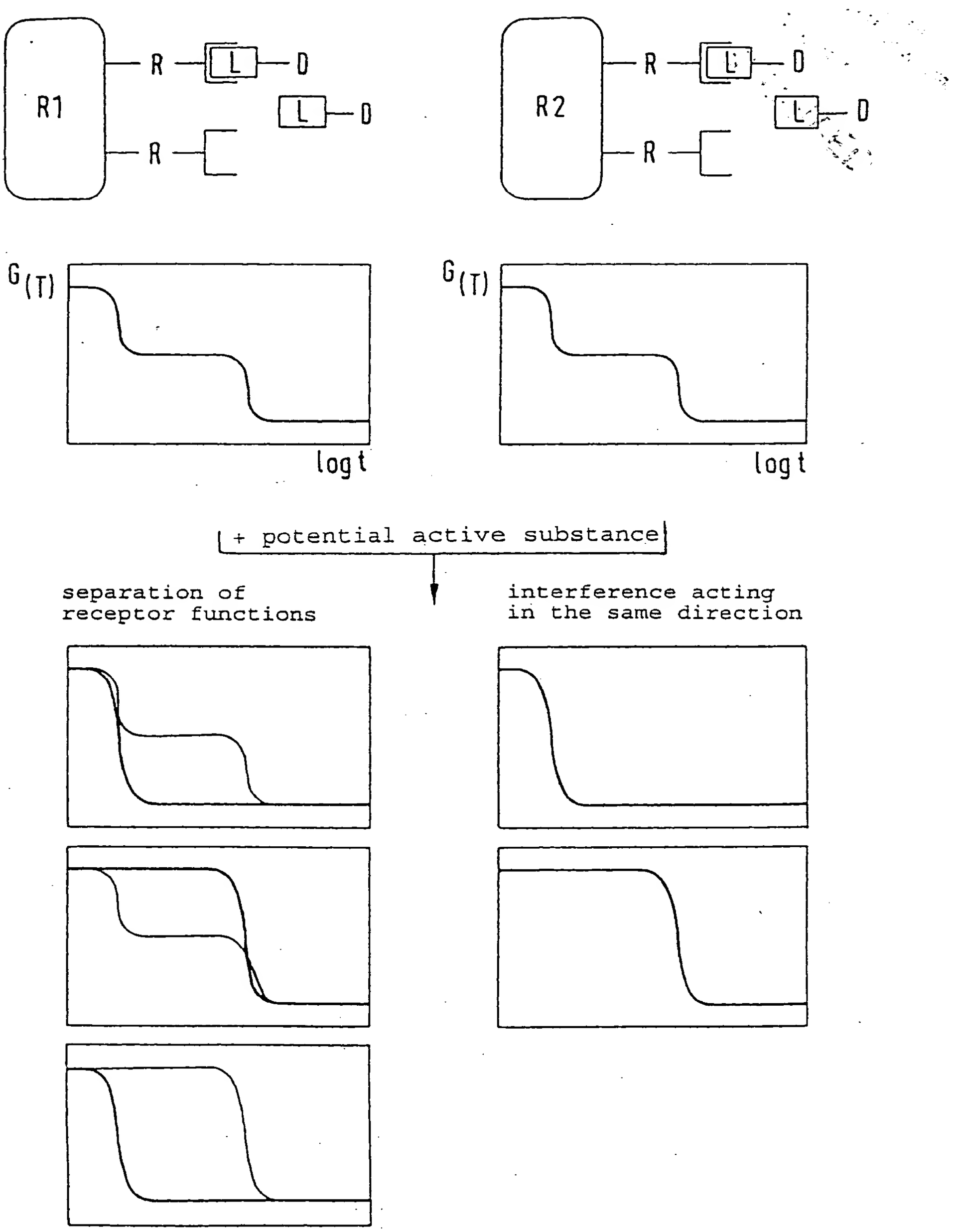

Receptor Assay (2)
R1
R
L
D
L
D
R
R2
R
L
D
L
D
R
G(T)
log t
G(T)
log t
+ potential active substance
separation of
receptor functions
interference acting
in the same direction

FIG. 3

FCS Analysis with Multi Well Sheets

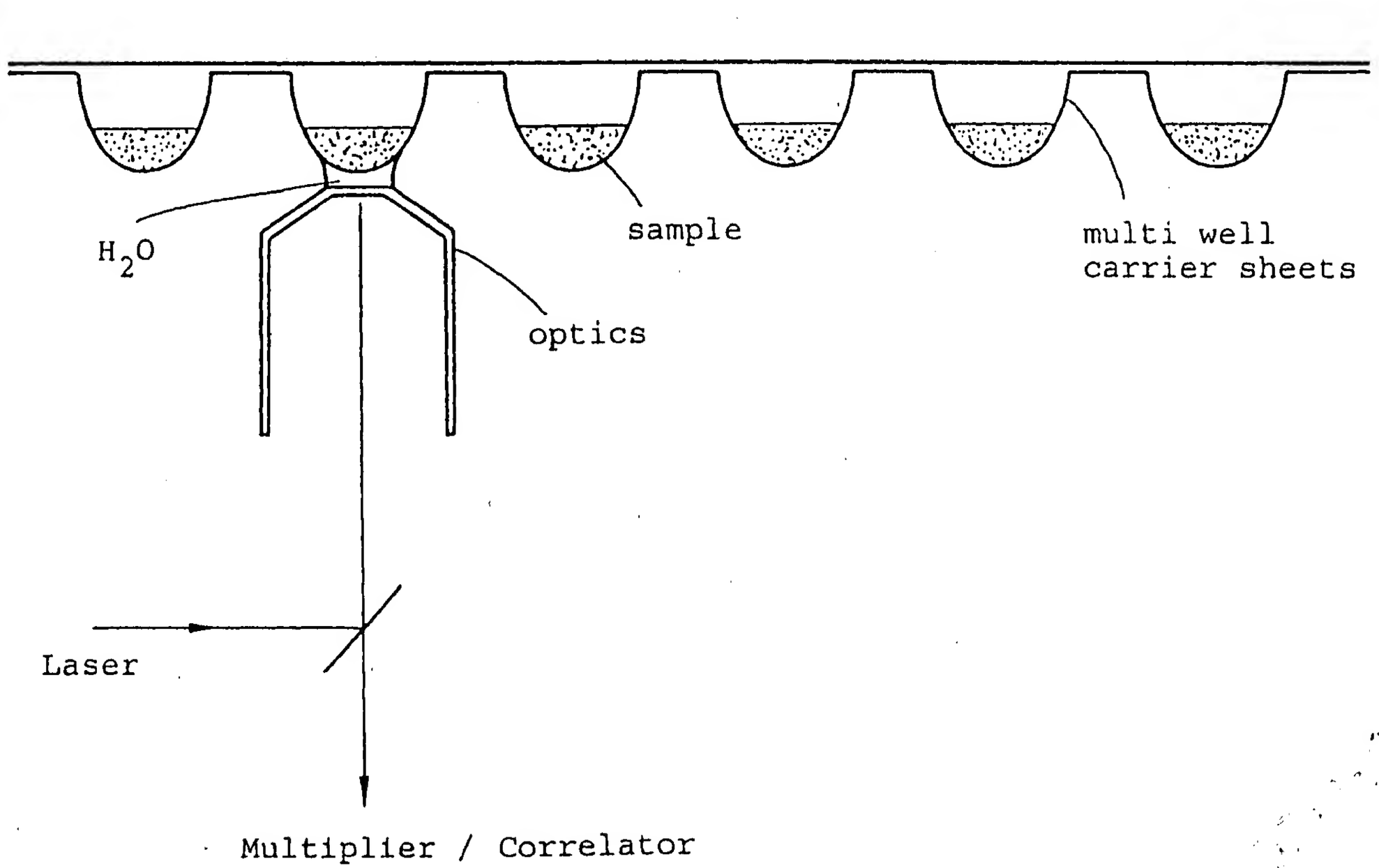


FIG. 4

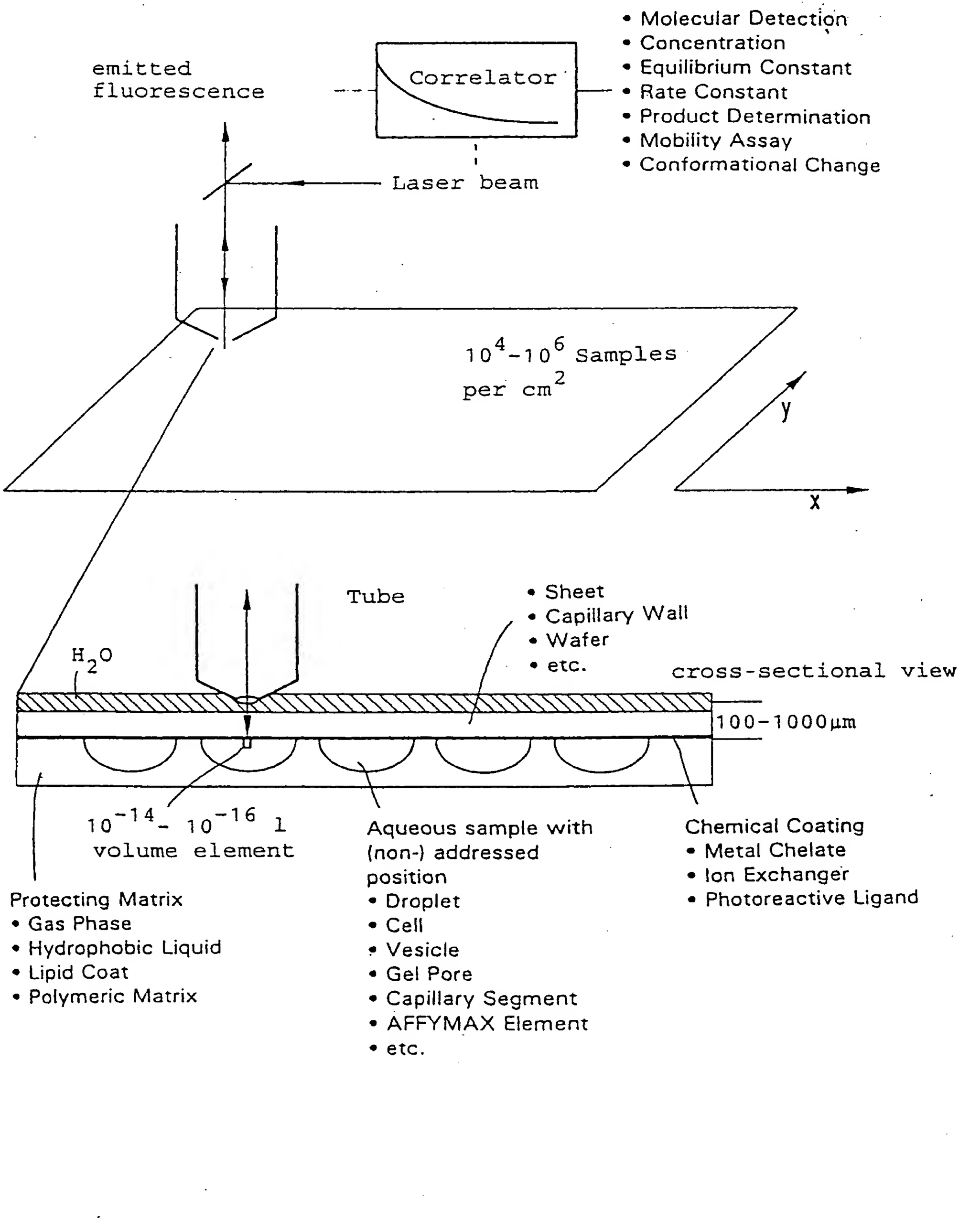

FCS - Determination of the Fitness of Mutants
emitted fluorescence
Correlator
• Molecular Detection
• Concentration
• Equilibrium Constant
• Rate Constant
• Product Determination
• Mobility Assay
• Conformational Change
Laser beam
10^4-10^6 Samples per cm^2
y
x
Tube
• Sheet
• Capillary Wall
• Wafer
• etc.
H_2O
cross-sectional view
100-1000µm
10^{-14}- 10^{-16} l volume element
Aqueous sample with (non-) addressed position
• Droplet
• Cell
• Vesicle
• Gel Pore
• Capillary Segment
• AFFYMAX Element
• etc.
Chemical Coating
• Metal Chelate
• Ion Exchanger
• Photoreactive Ligand
Protecting Matrix
• Gas Phase
• Hydrophobic Liquid
• Lipid Coat
• Polymeric Matrix

FIG. 5

Detection of Molecules on stationary structures through relative temporal change of the positional coordinates of the measuring volume

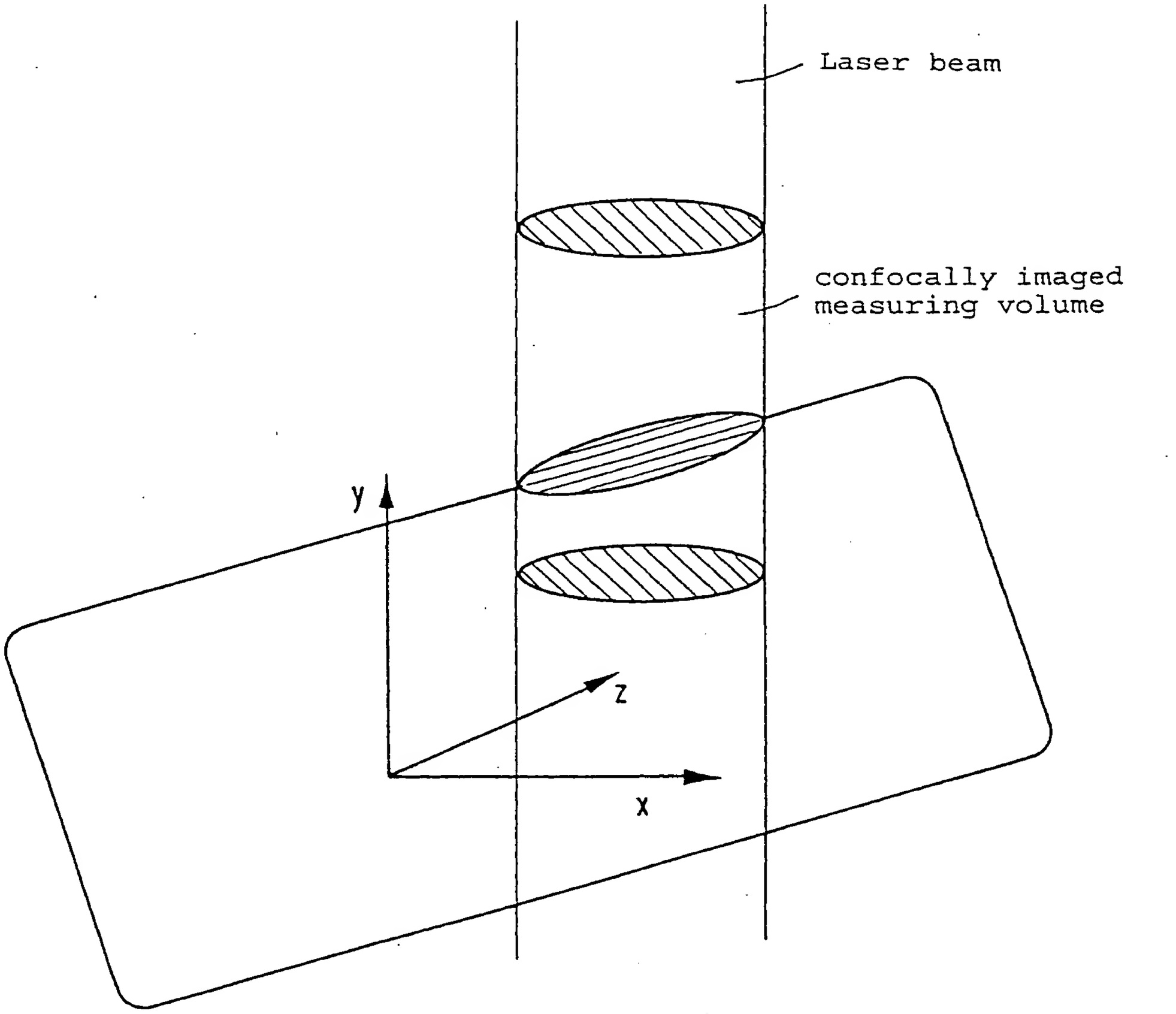


FIG. 6

Detection of Single Molecules
in the Electric Trap

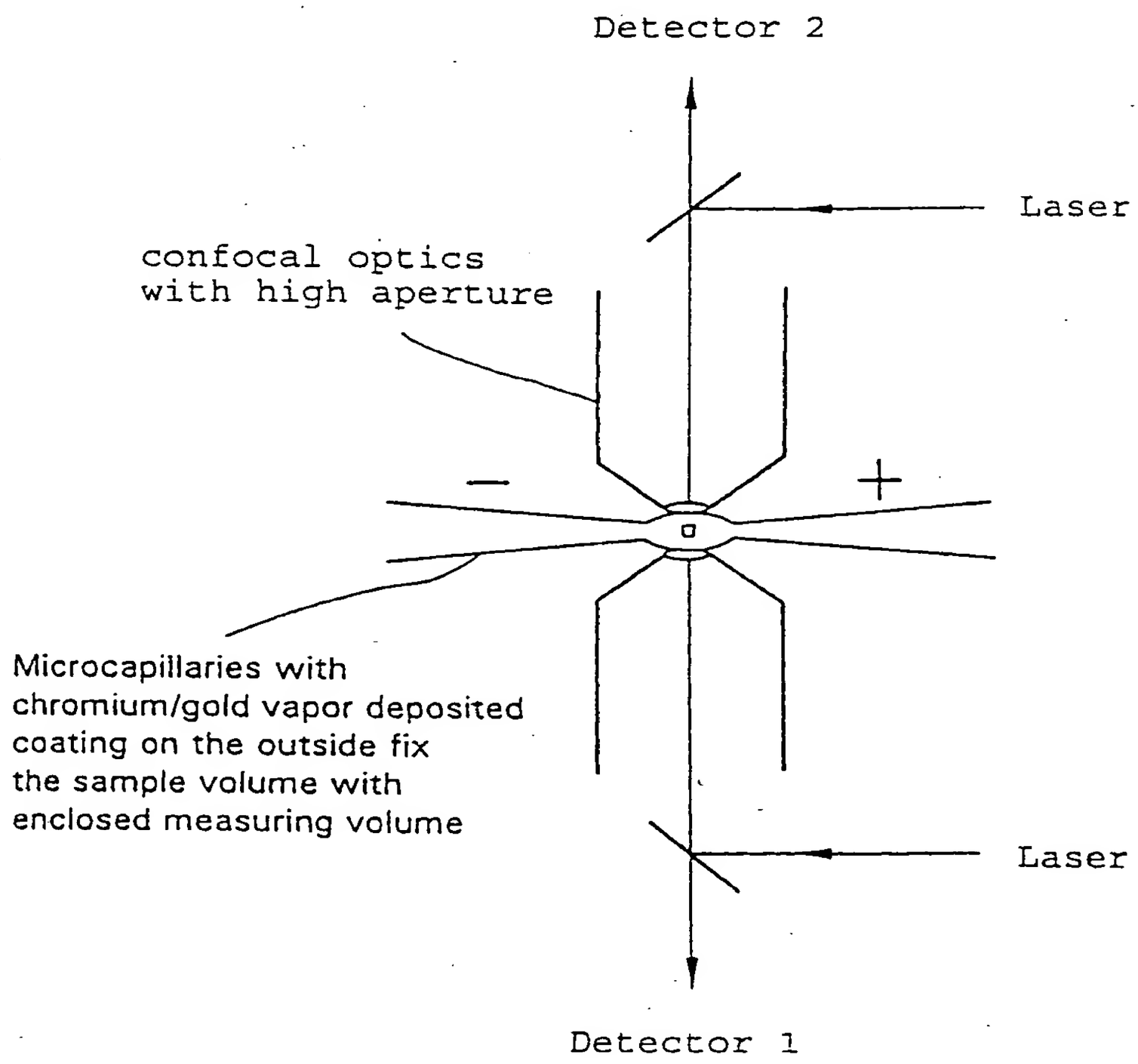
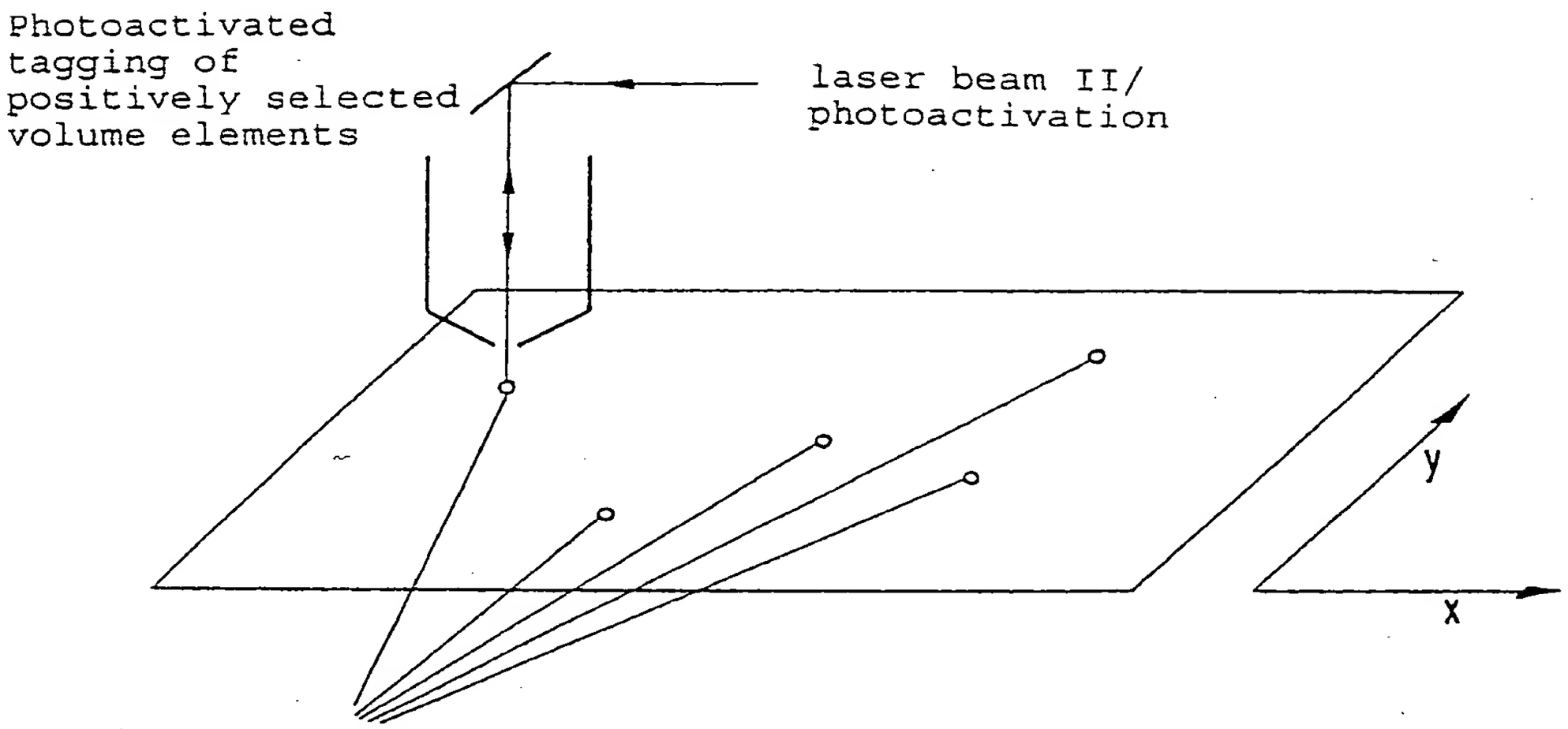


FIG. 7

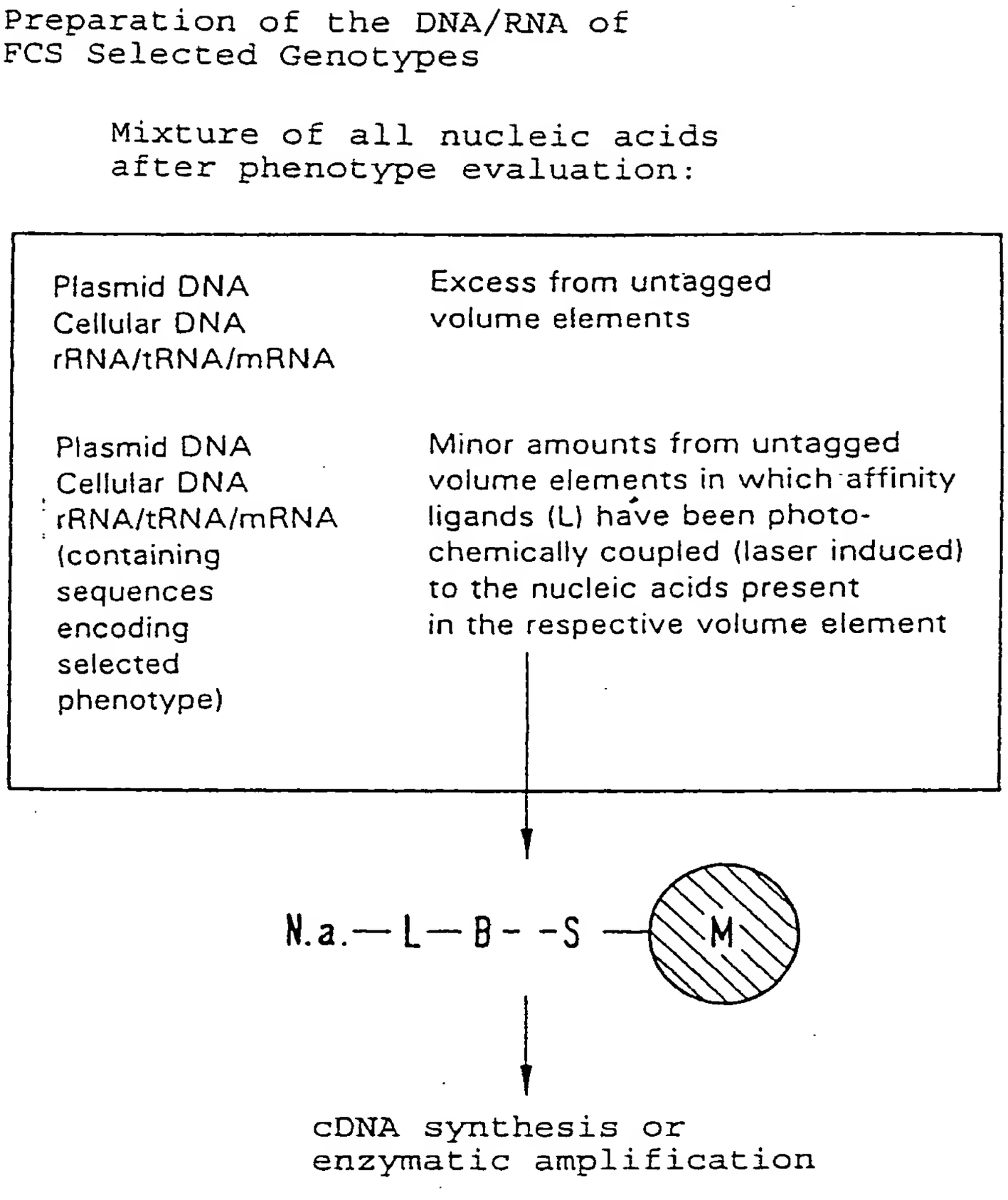
FCS - Tagging of the
Selected Genotypes



a) Physical access to optically
tagged volume elements

b) Light induced linking of the nucleic acid
of selected volume elements to affinity ligands
- at the carrier surface
- to soluble ligands

FIG. 8



N.a.; Nucleic acid.
L; Ligand with specific nucleic acid affinity which can be photochemically coupled covalently and preferably reversibly to a nucleic acid (e.g. a psoralen derivative). The ligand is preferably linked to a substituent which allows for subsequent enrichment of the nucleic acids. For instance, this can be a hydrophobic substituent to purify nucleic acids by reversed phase chromatography. For affinity chromatography, substituents such as biotin (B) are the obvious suitable ones so that the nucleic acids can be enriched through (strept)avidin complexing (S) with appropriately modified magnetobeads (M) or surfaces.

FIG. 9

FLUCS Analysis of Complex Mixtures of Substances after Chromatographic Separation in Fractions

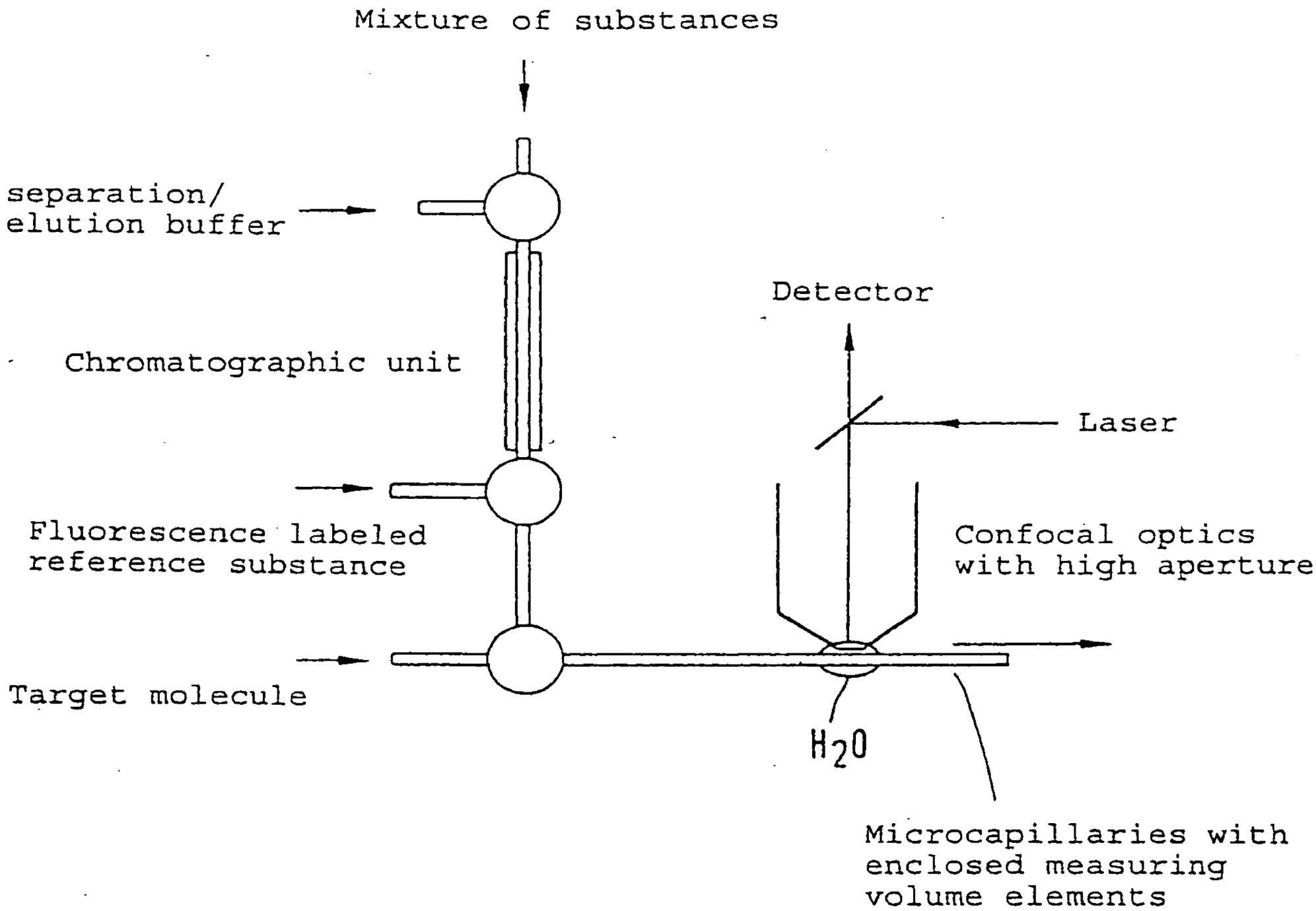


FIG. 10

Laser Correlation Microscope

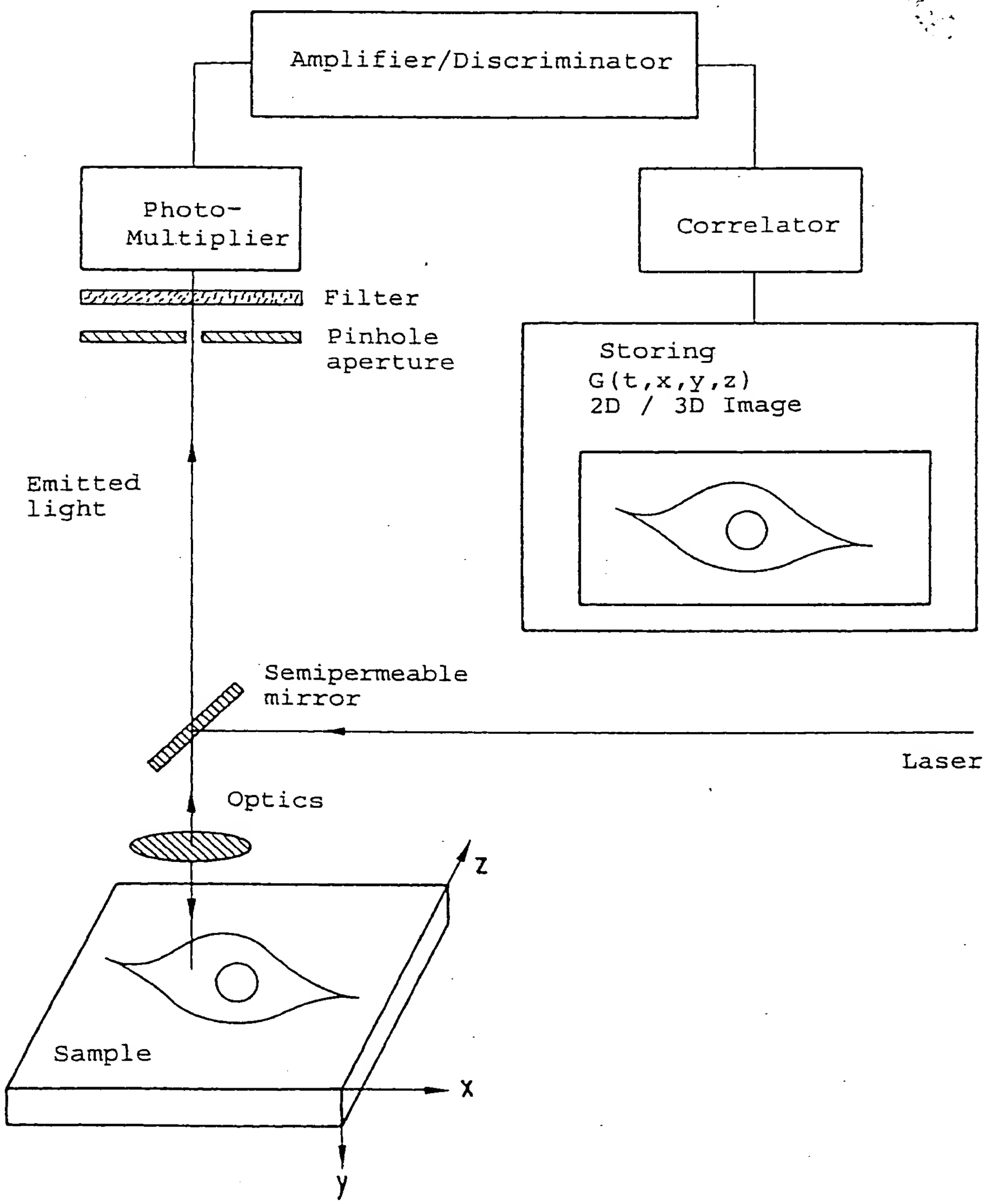
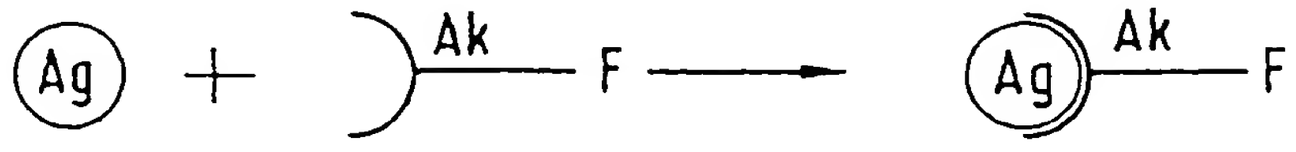


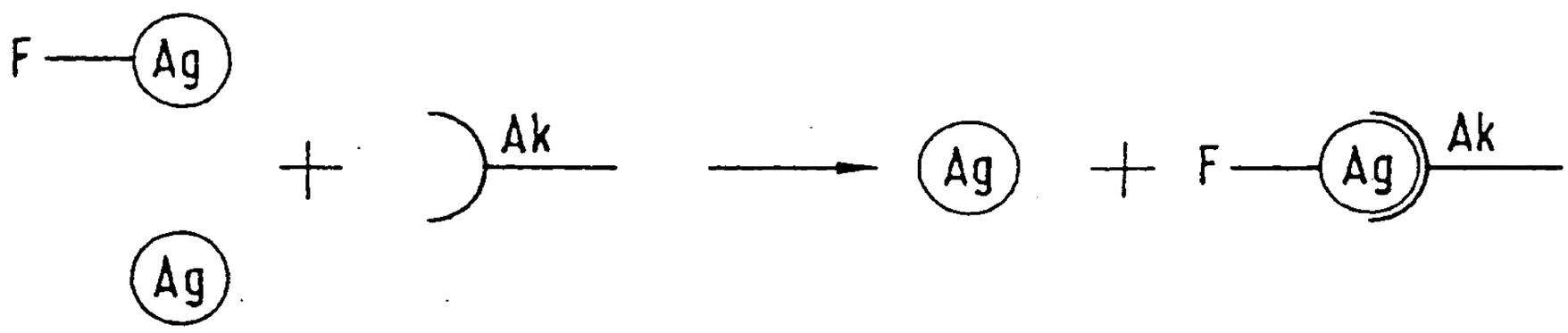
FIG. 11

Selection of Possible Assays

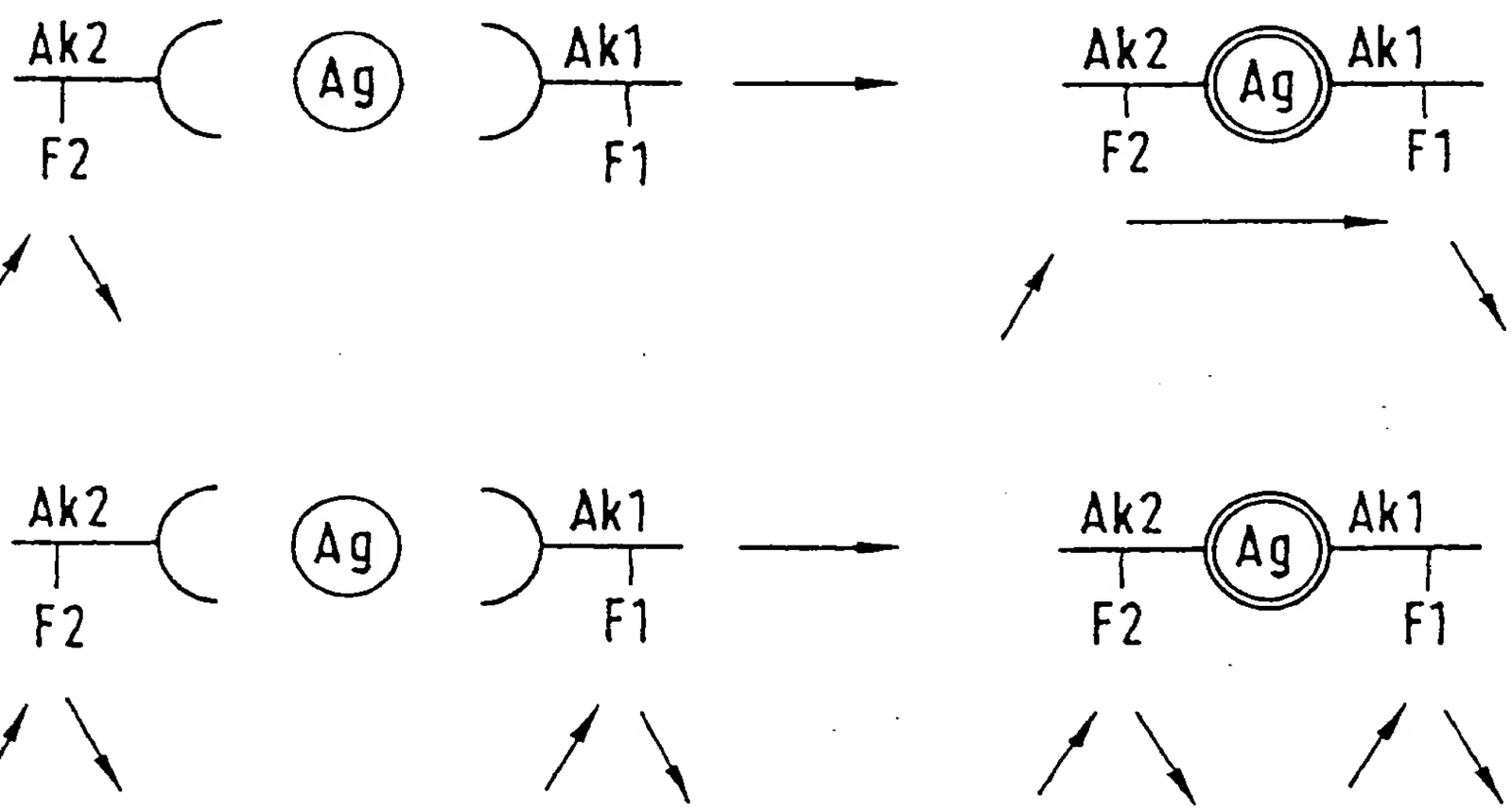


(A)

(B)



(C)



(D)

(E)

FIG. 12

Electrophoresis Cell

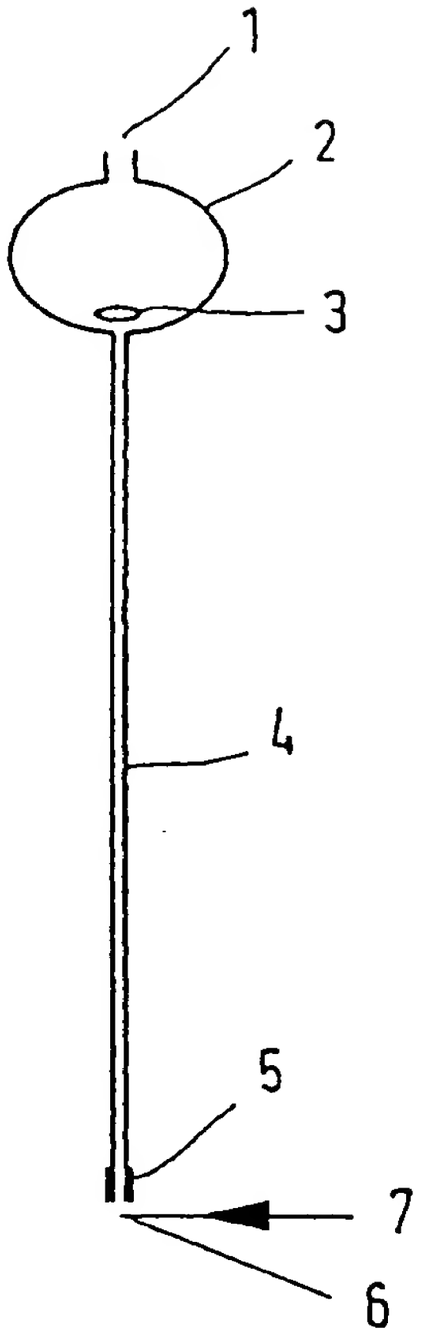


FIG. 13

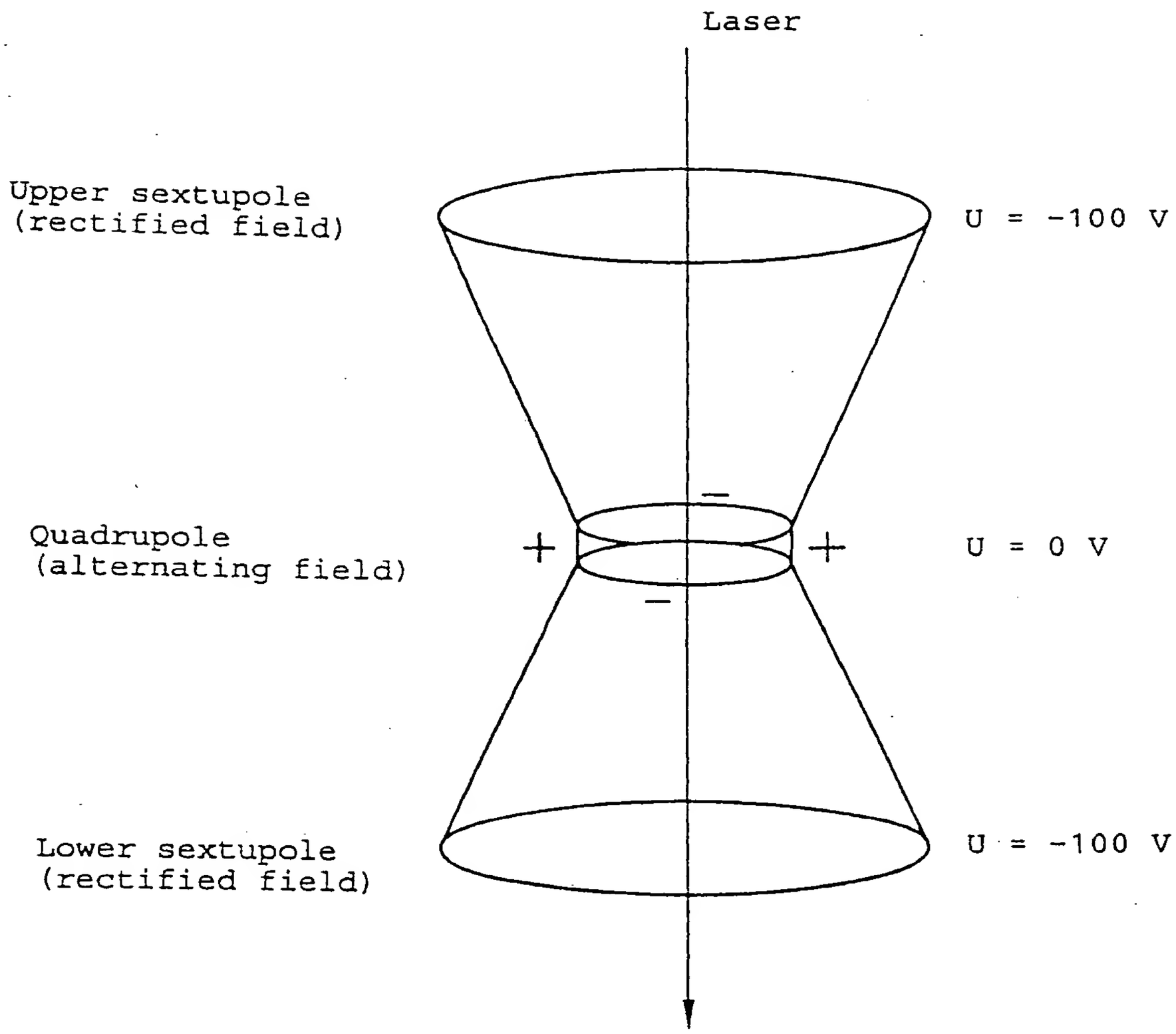

Laser
Upper sextupole
(rectified field)
U = -100 V
Quadrupole
(alternating field)
U = 0 V
Lower sextupole
(rectified field)
U = -100 V

FIG. 14

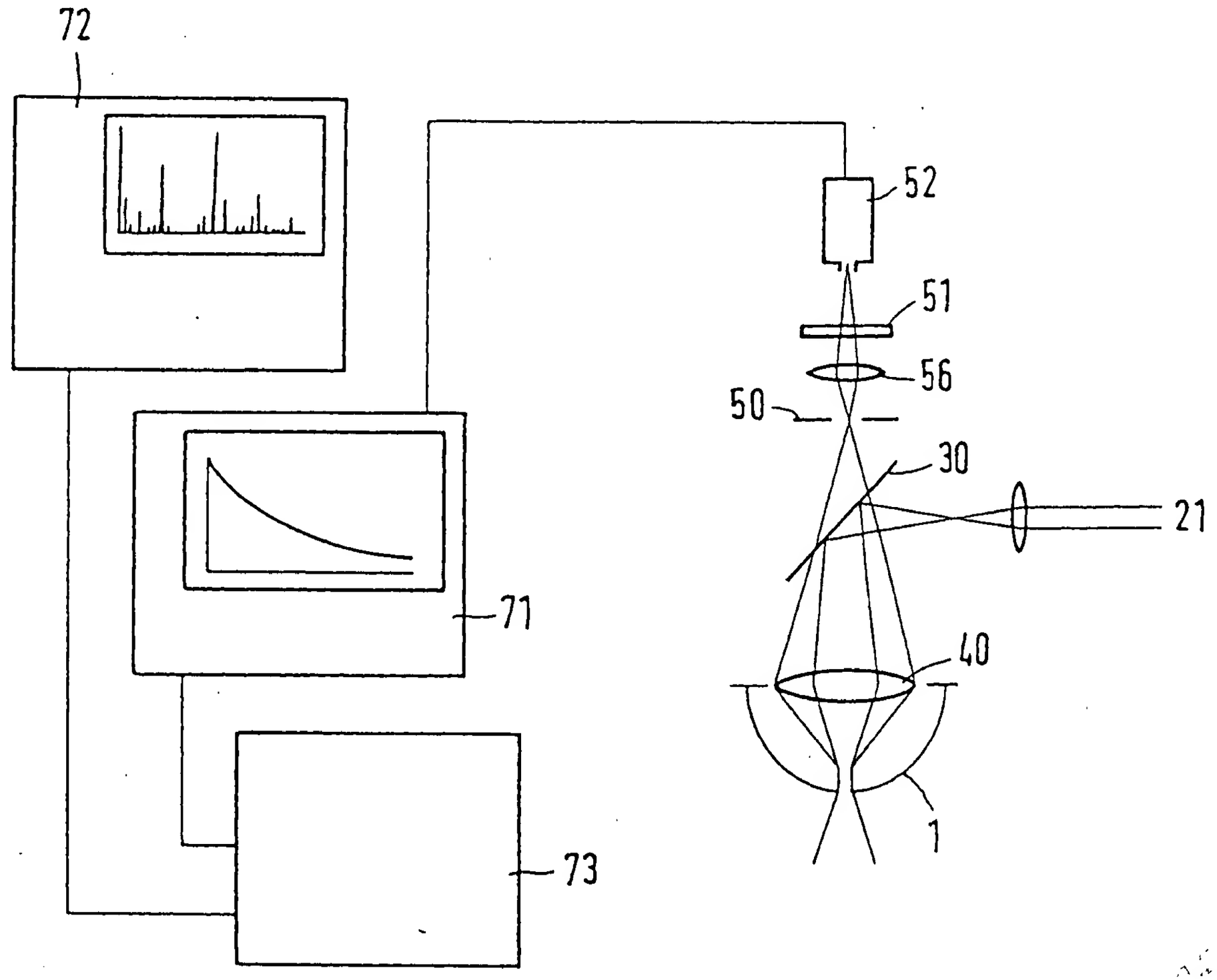


FIG. 15

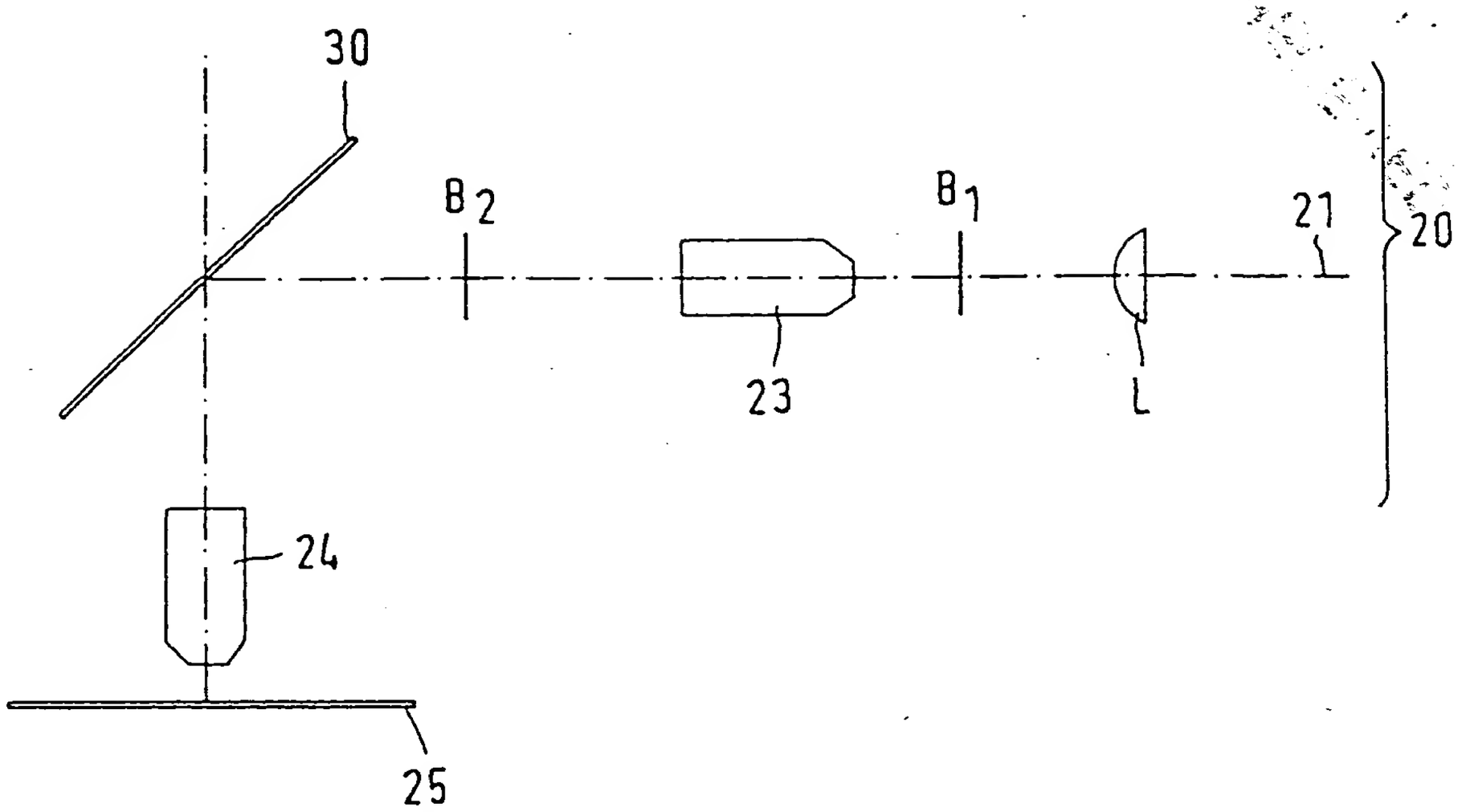


FIG. 16

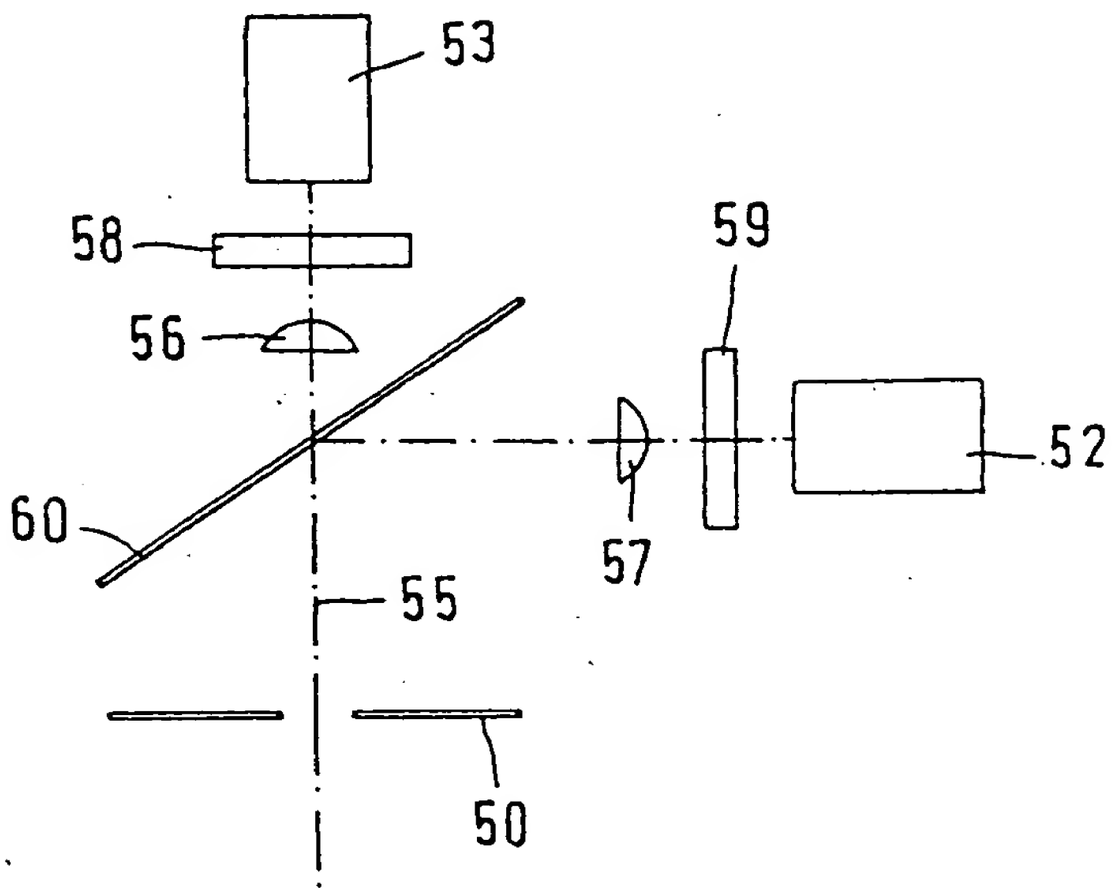


FIG. 17a

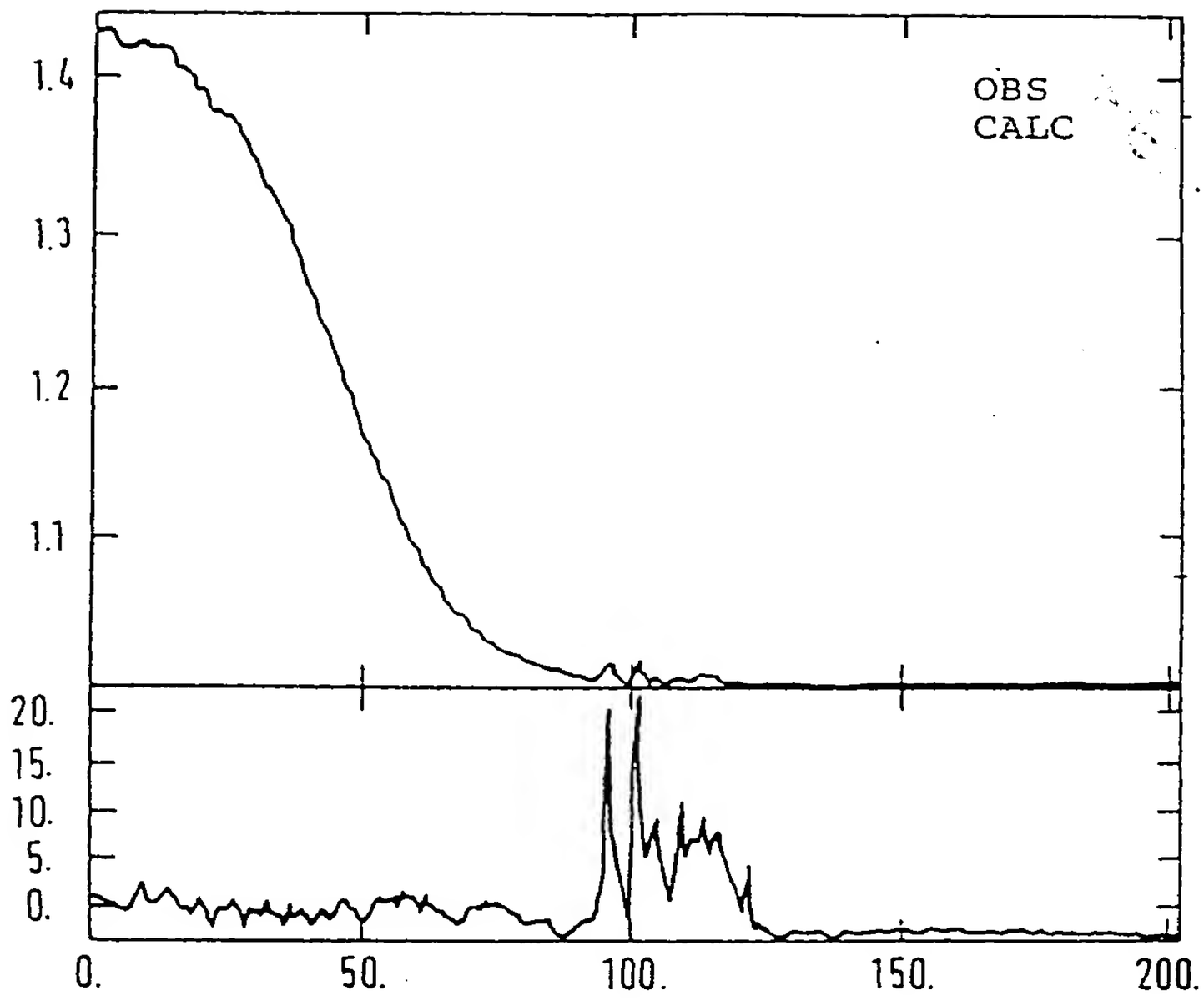


FIG. 17b

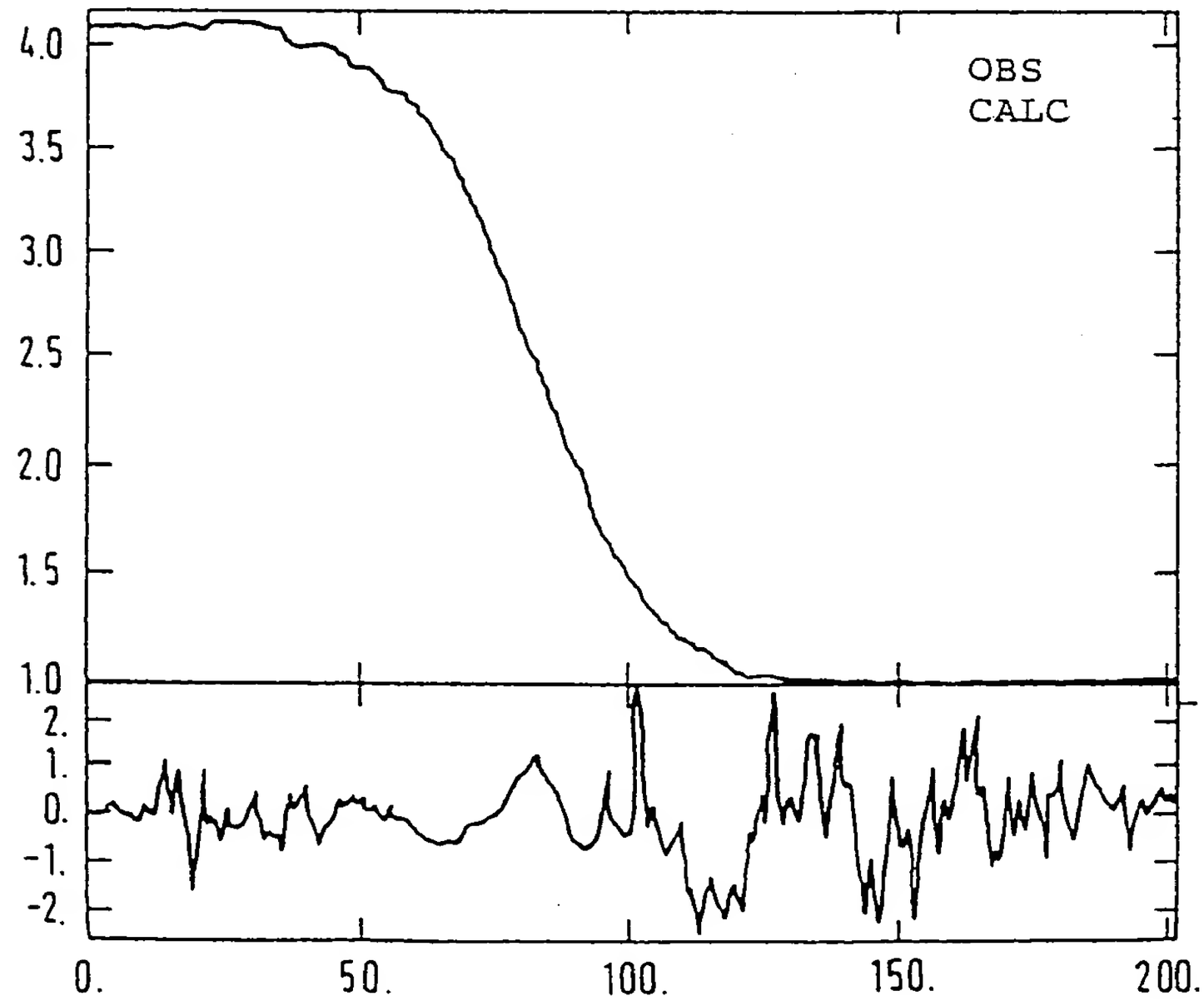


FIG. 18a

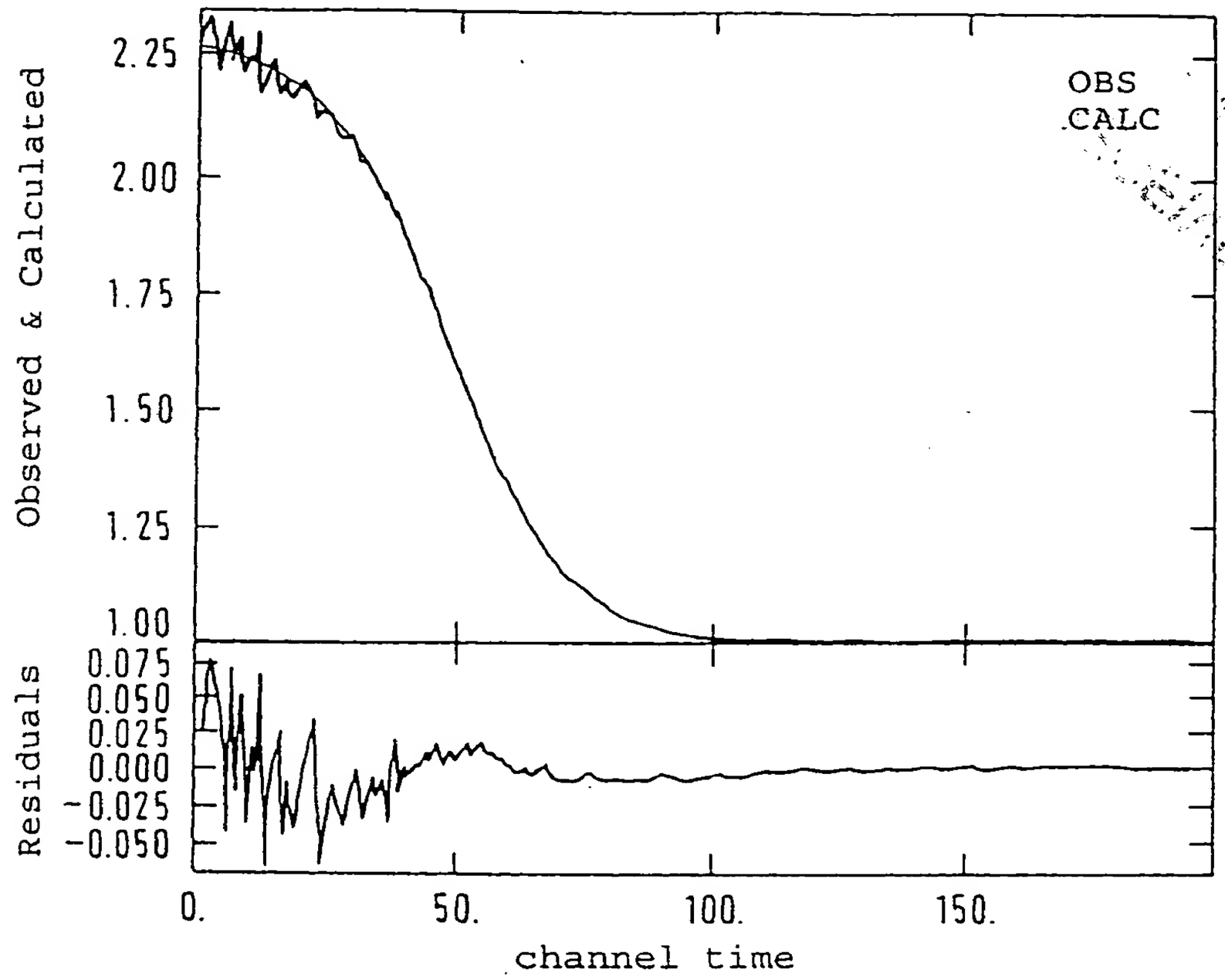


FIG. 18b

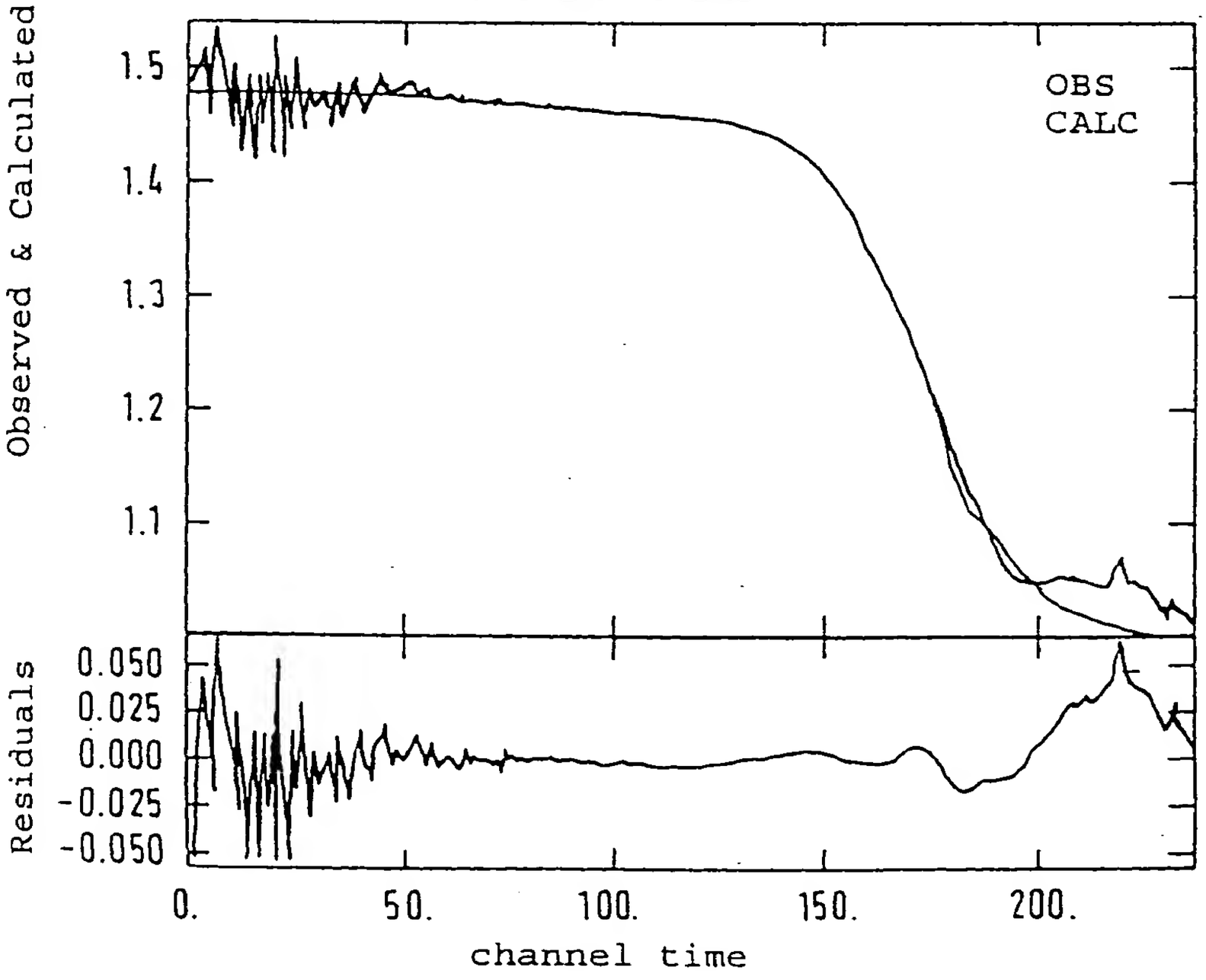


FIG. 18c

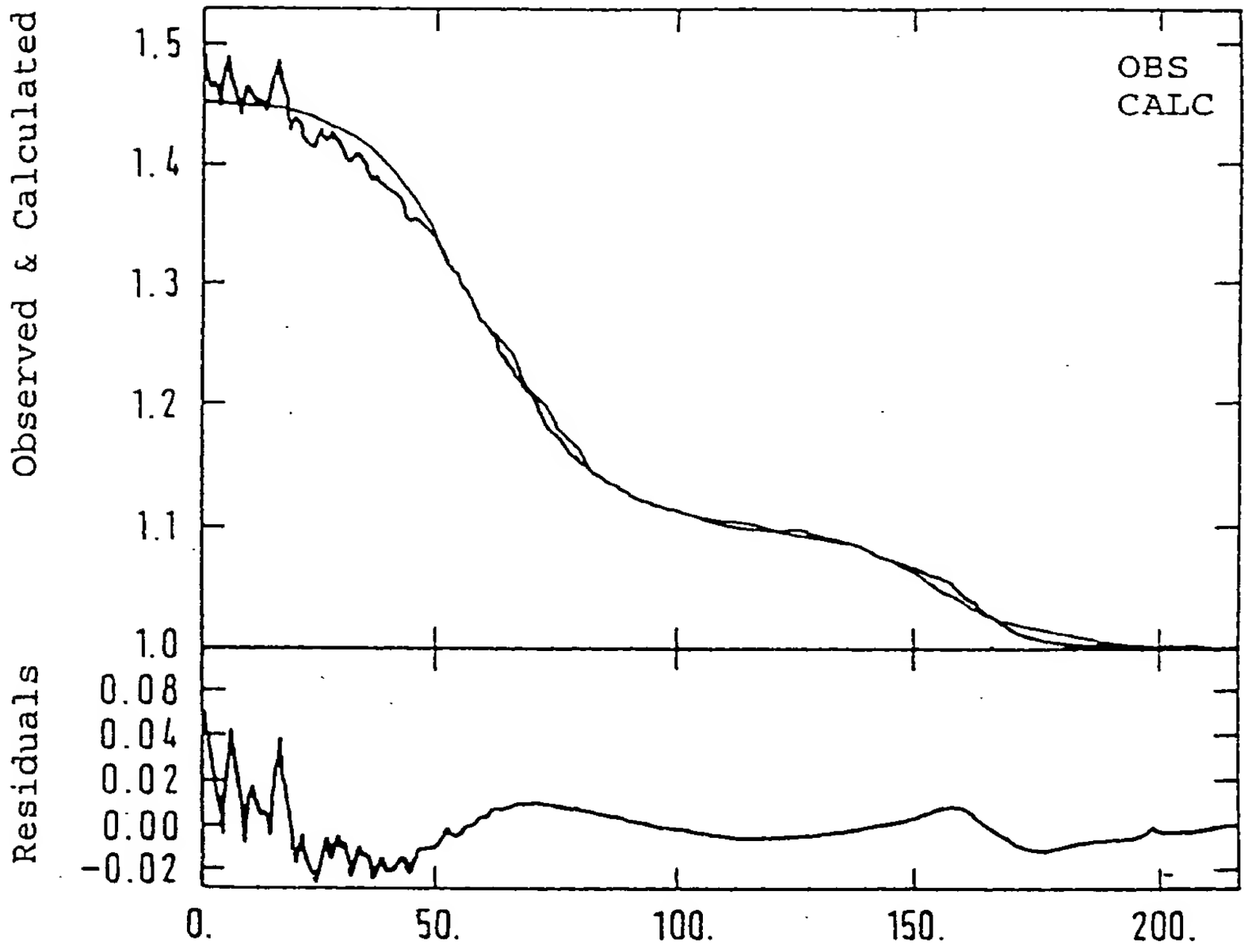
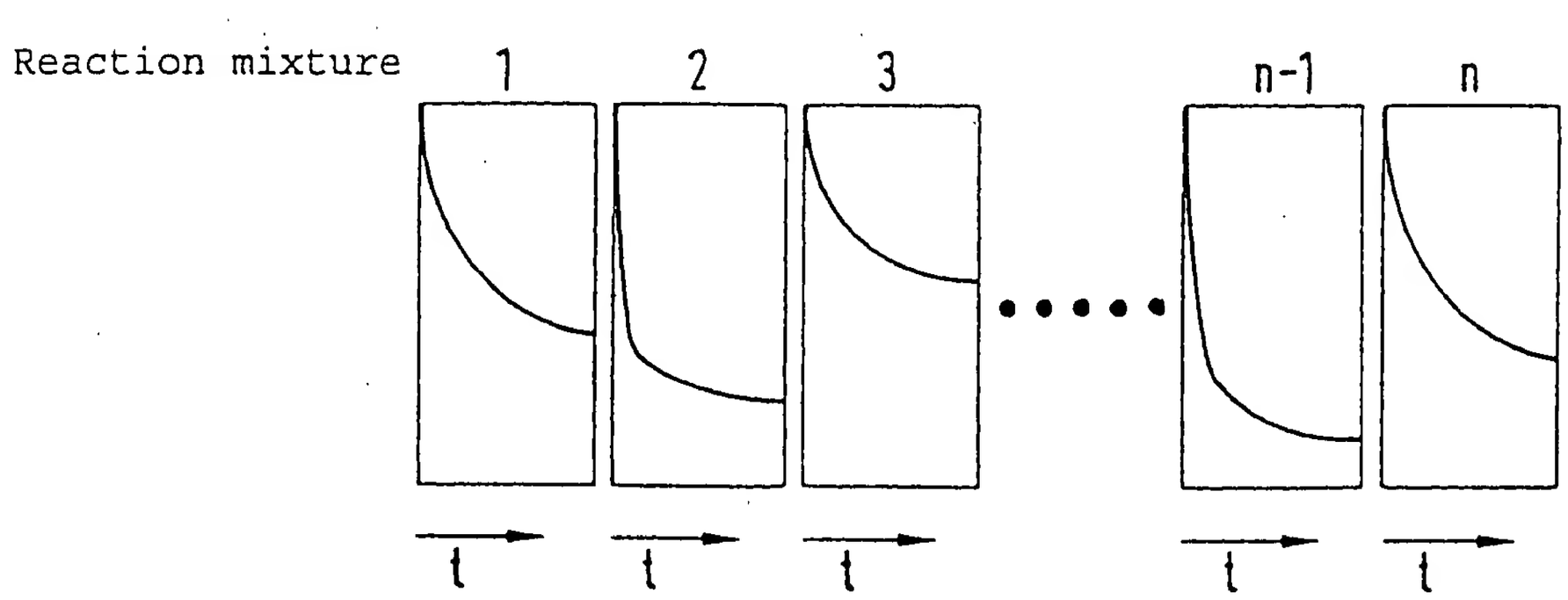

Observed & Calculated
1.5
1.4
1.3
1.2
1.1
1.0
OBS
CALC
Residuals
0.08
0.04
0.02
0.00
-0.02
0.
50.
100.
150.
200.
channel time

FIG. 19

Determination by FCS of the Dissociation Behavior
of Complexes in Experiments Performed in Parallel



Different Embodiments of the Electric Trap According to the Invention

FIG. 20a

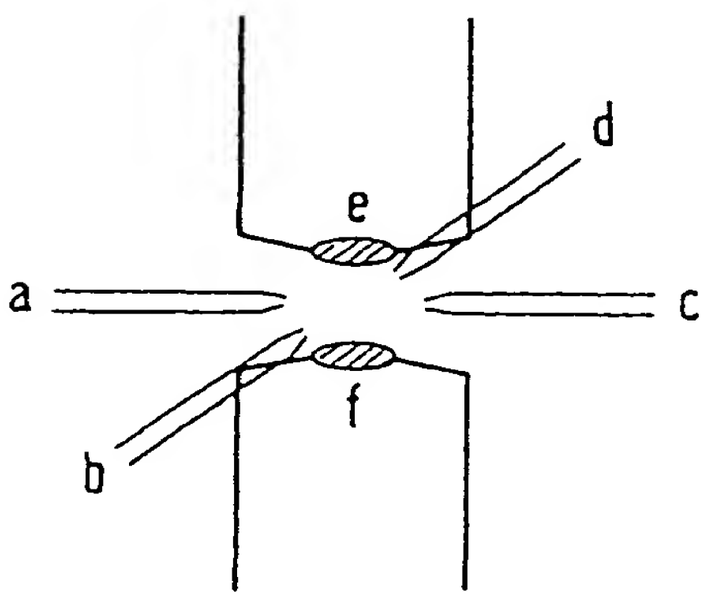


FIG. 20b

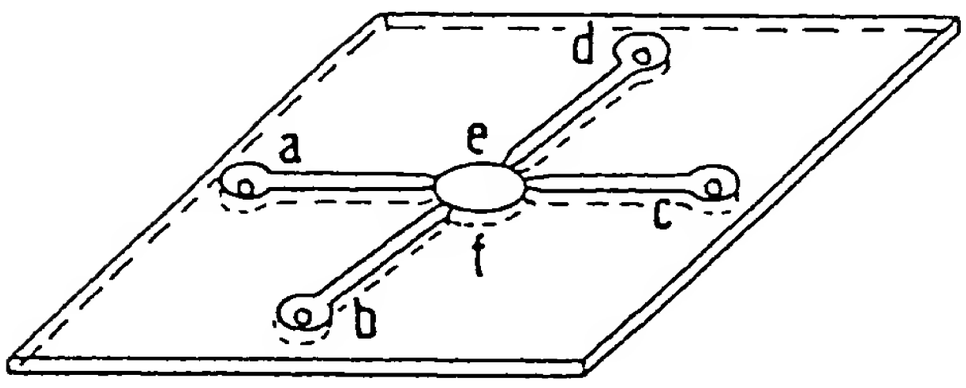
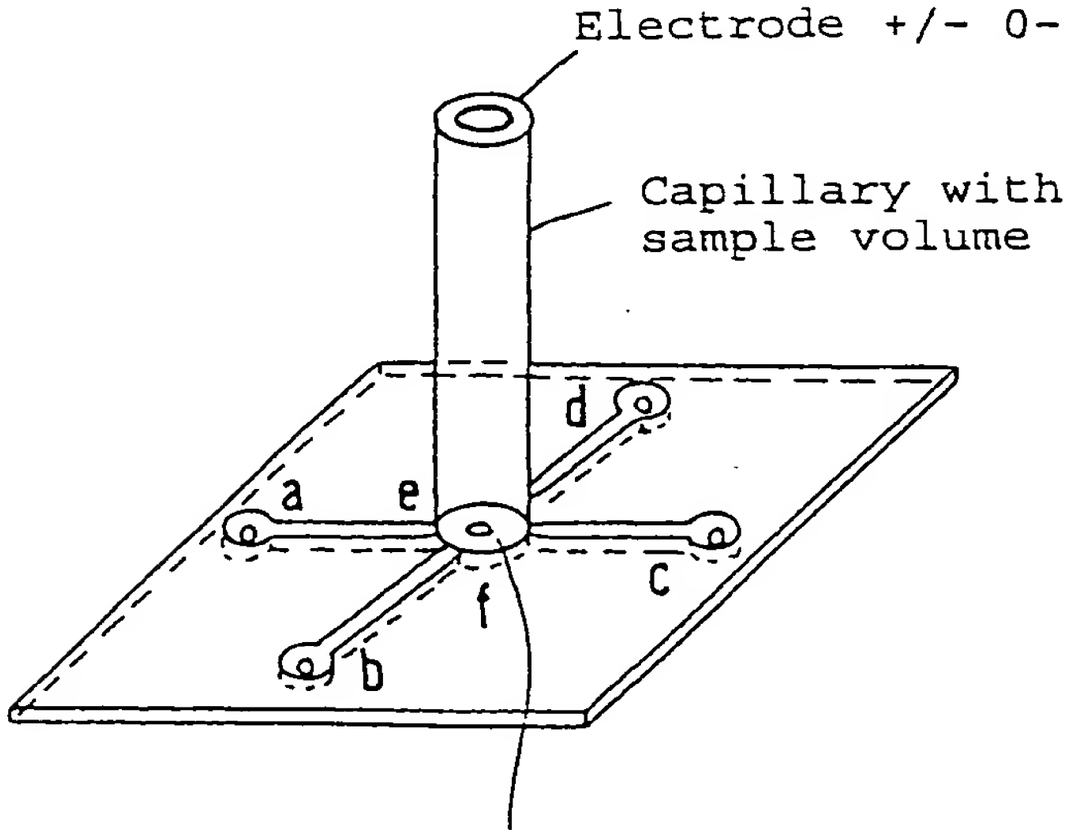


FIG. 20c

Electrode +/- 0-100 V



Collecting electrode with earthing (potential 0 V) and Pinhole for ions to pass into the quadrupolar field

Molecular Detection

FIG. 21a

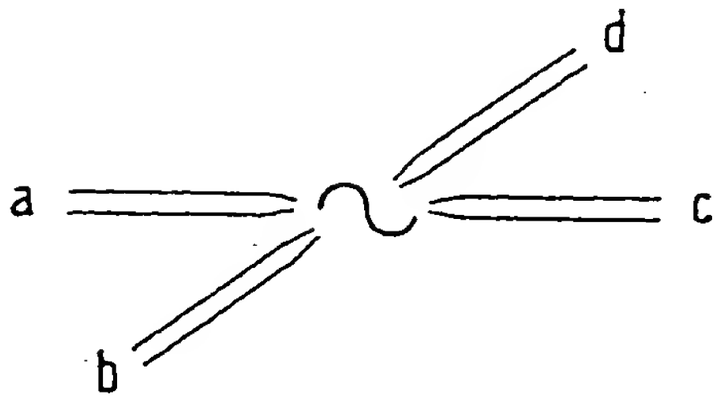


FIG. 21b

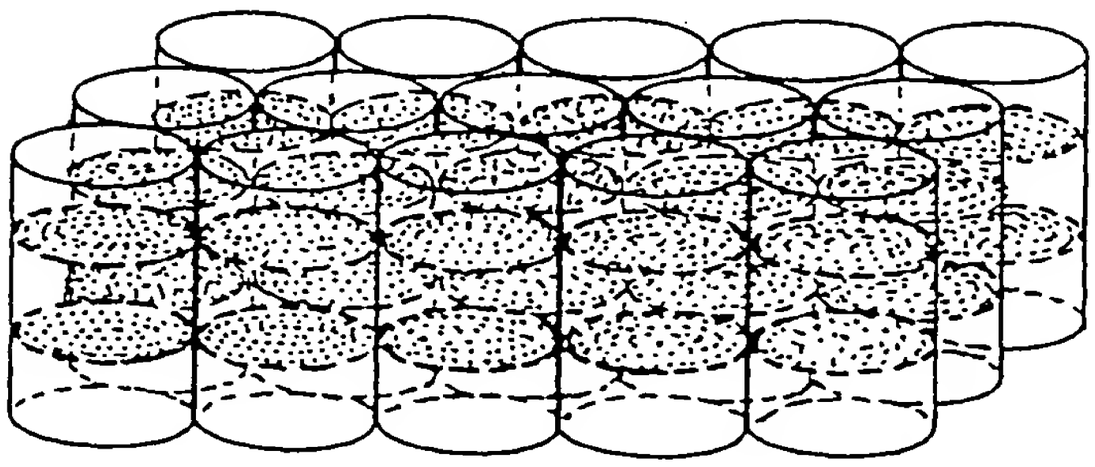


FIG. 22

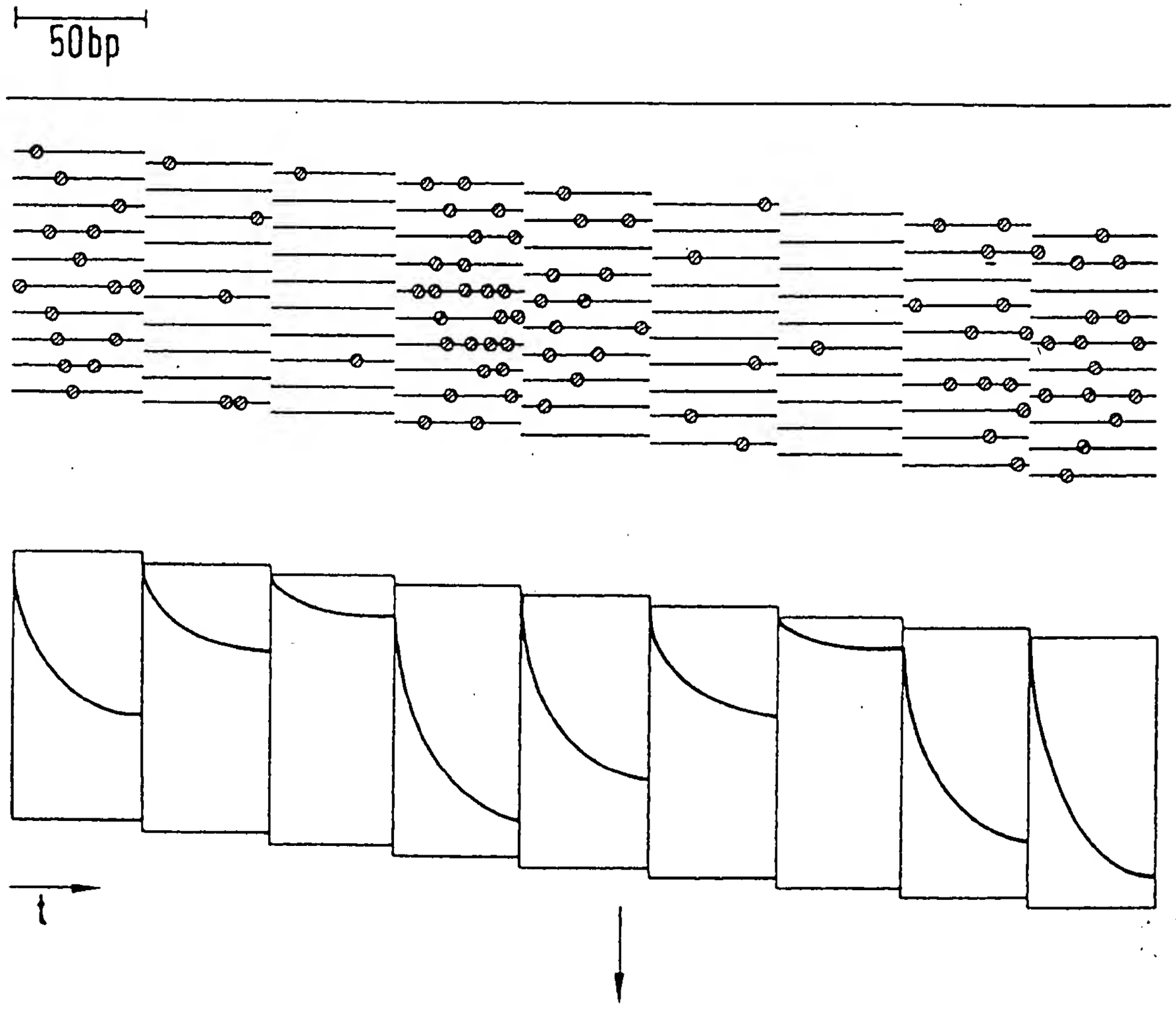
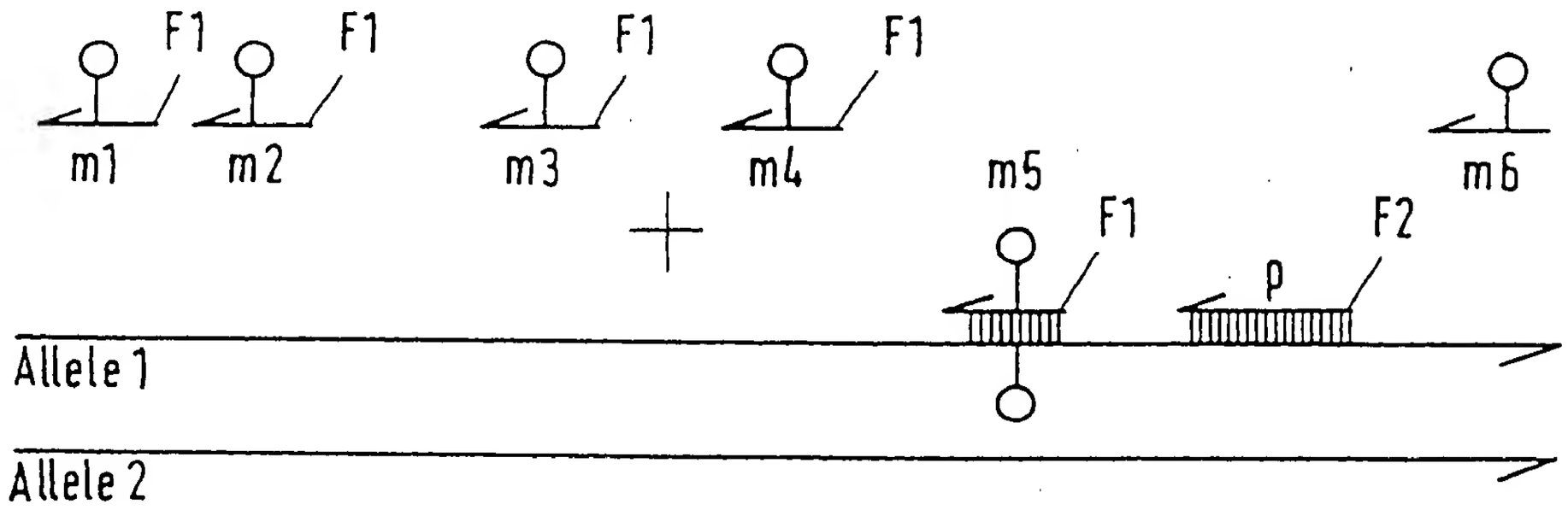


FIG. 23



Small Excitation Volumes (a) and
Small Measuring Volumes (b) and Small
Volumes with Parallel Measurements (c)

FIG. 24a

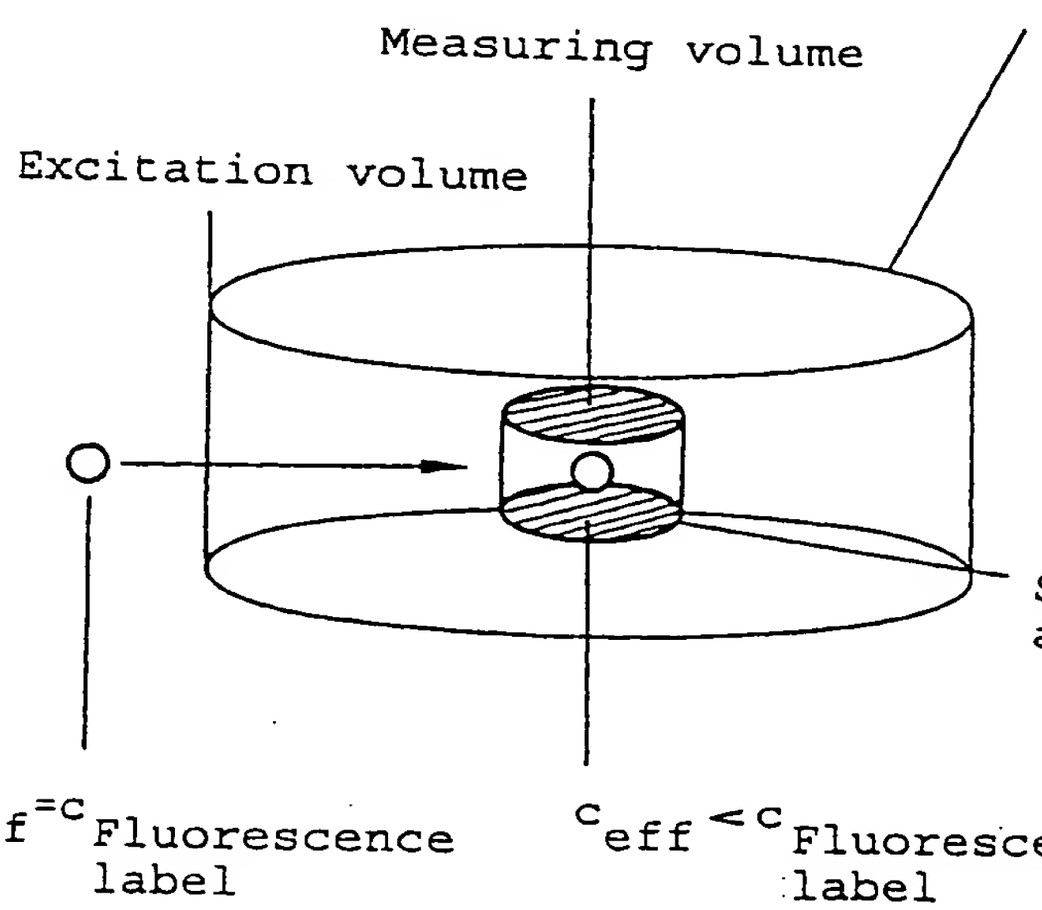


FIG. 24b

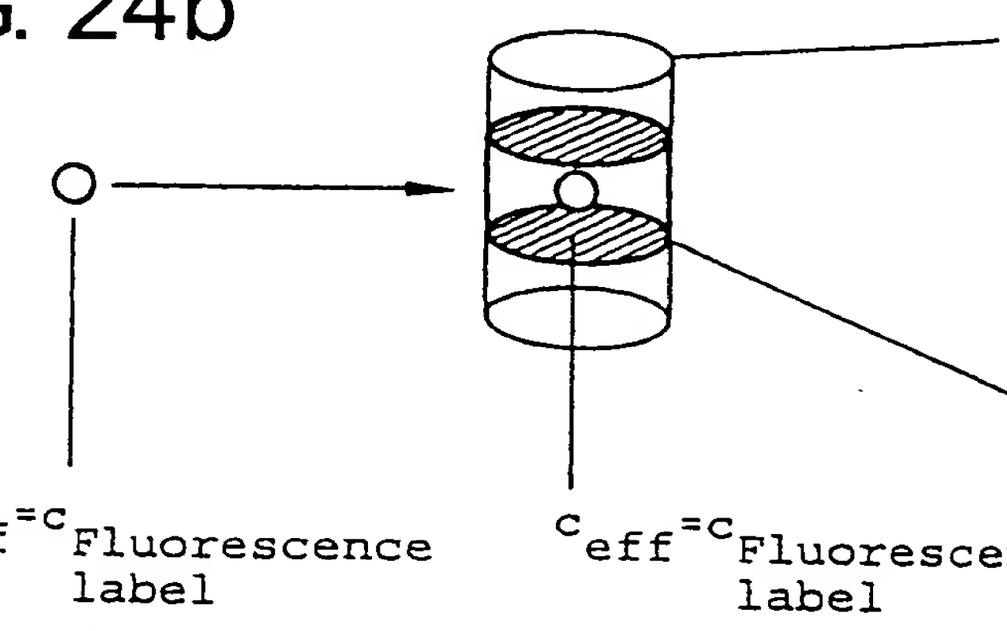


FIG. 24c

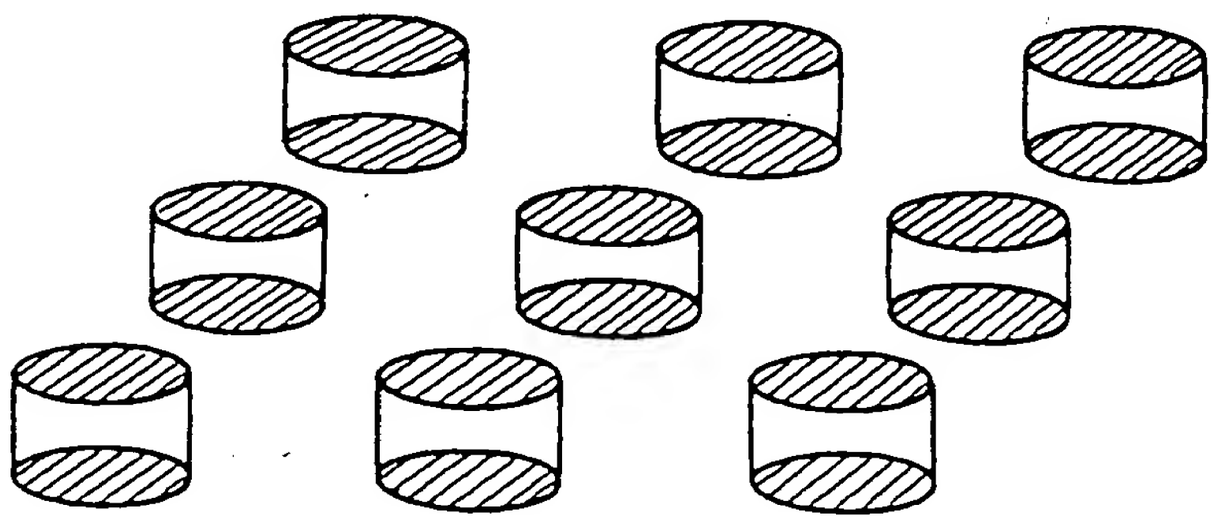


FIG. 25

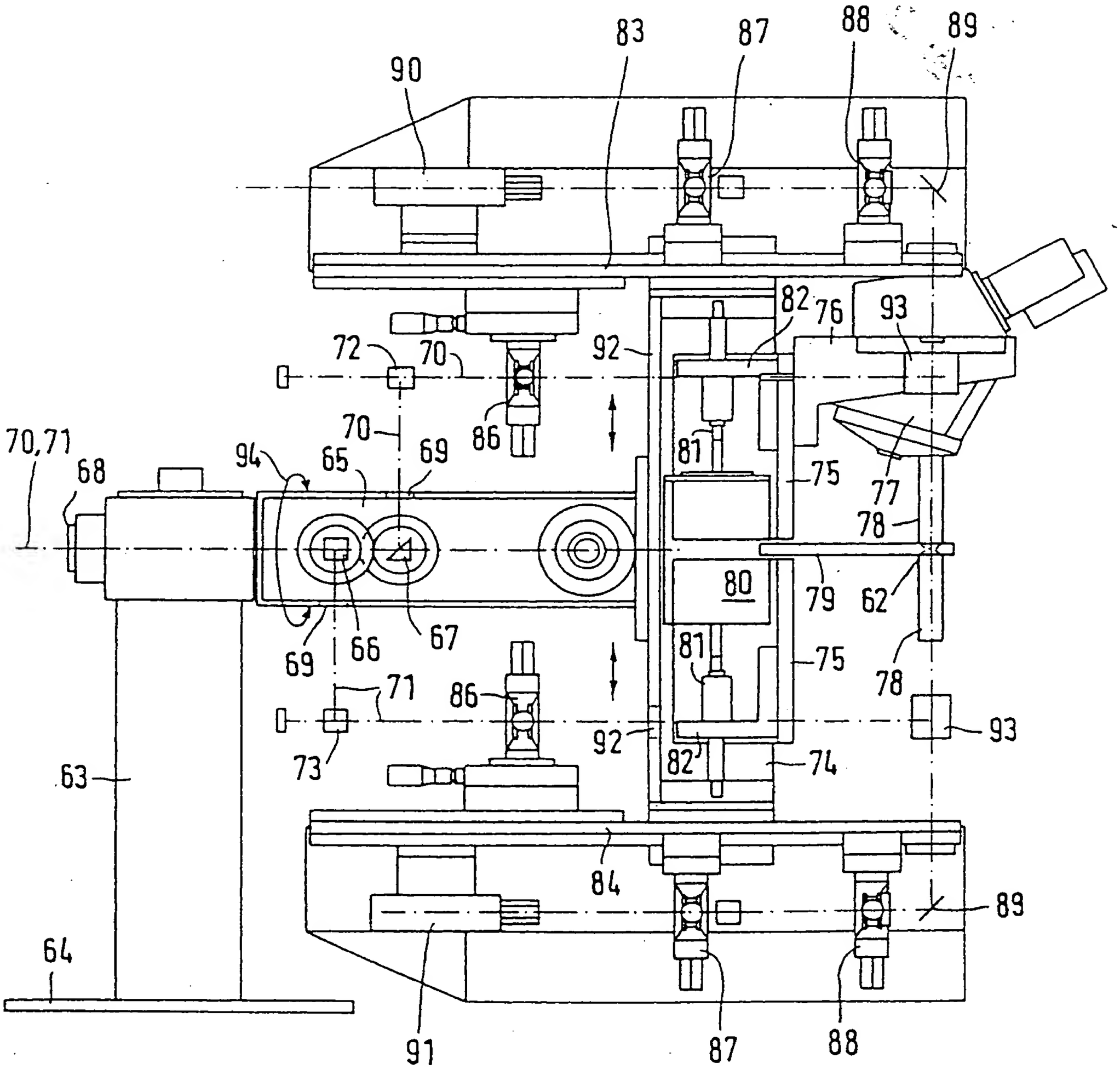

90
83
87
88
89
72
70
92
82
76
93
70
86
81
75
77
70,71
68
94
65
69
78
80
79
62
69
66
67
81
75
78
71
86
92
93
73
82
74
63
84
89
64
91
87
88

FIG. 26a

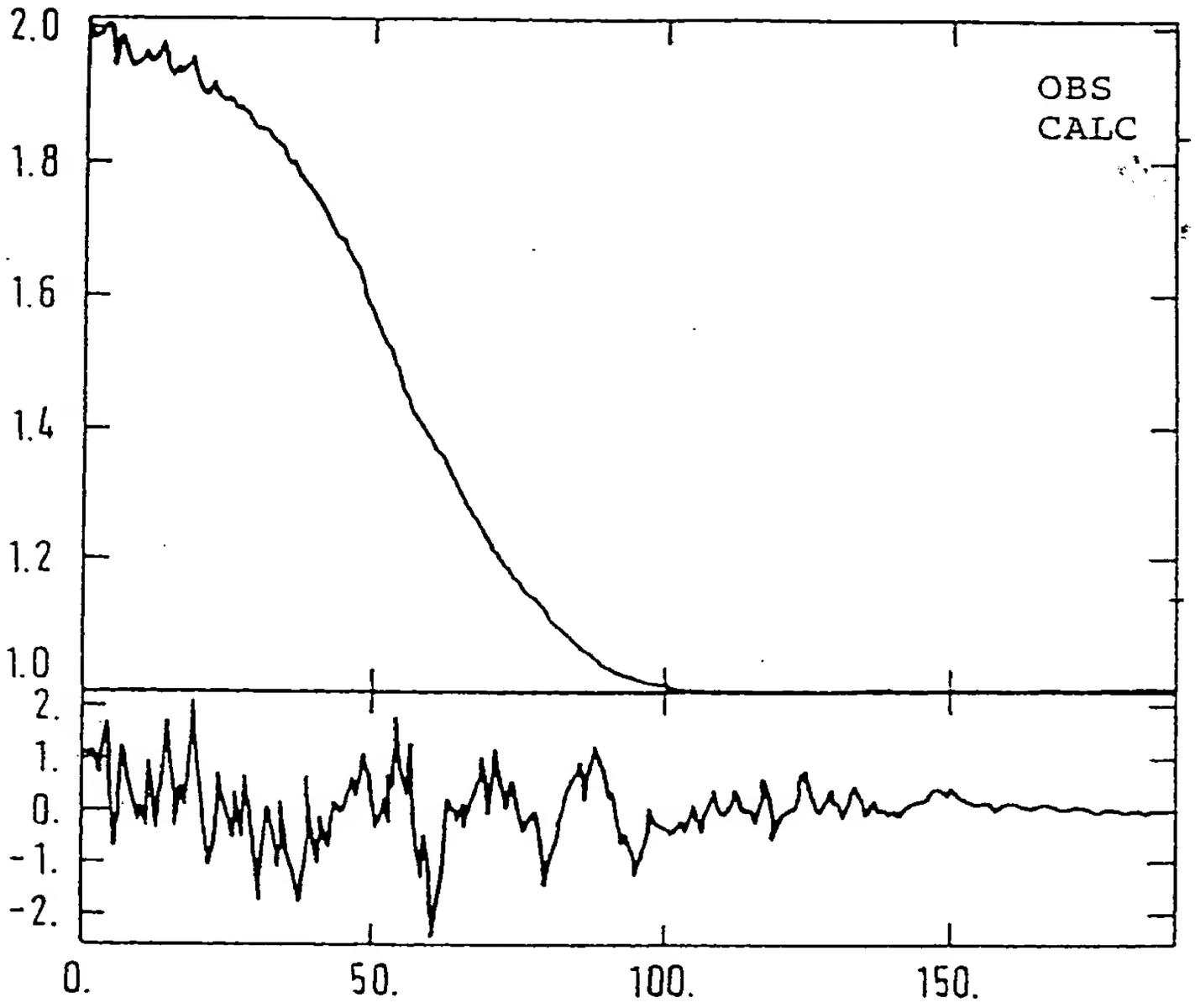


FIG. 26b

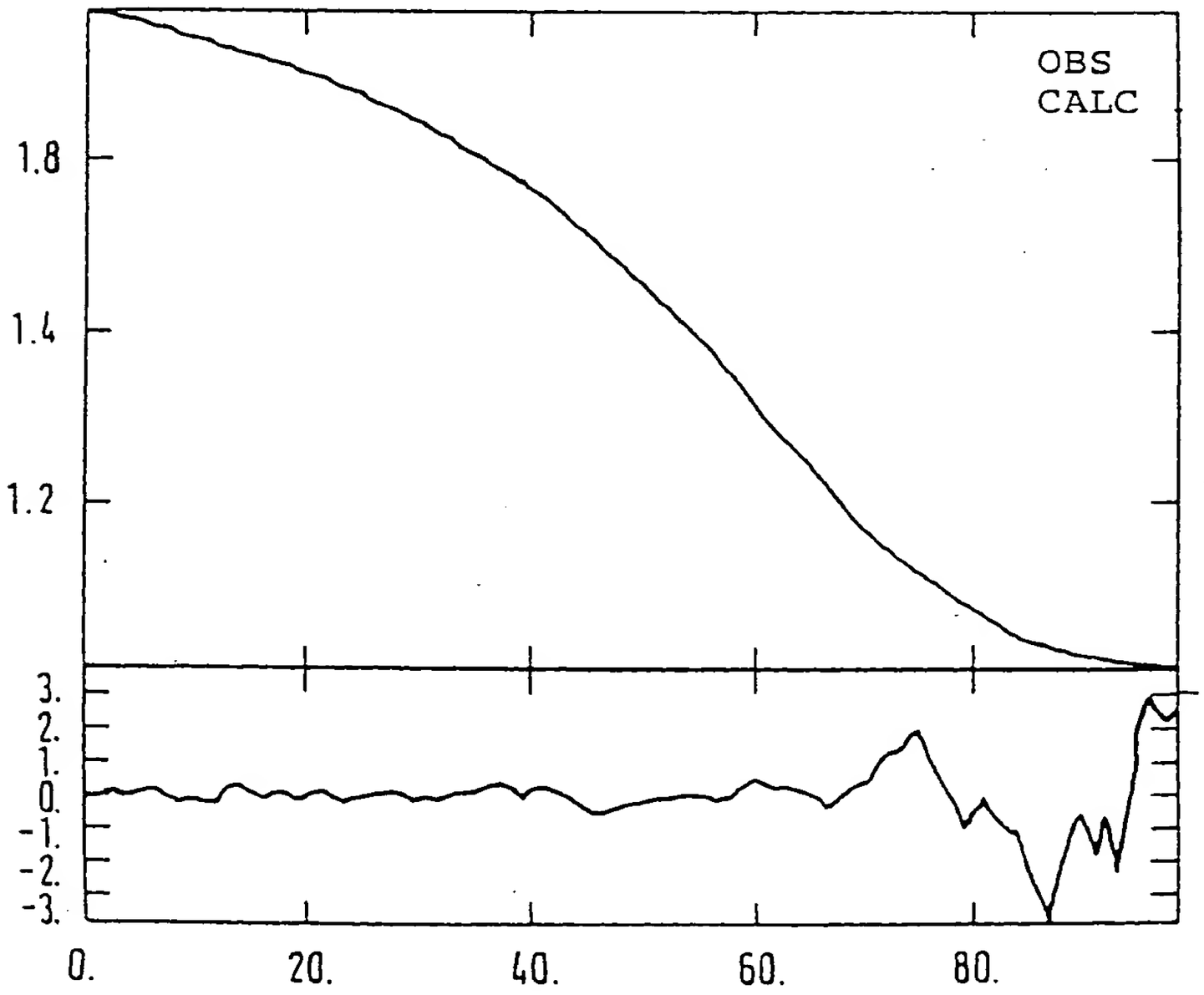


FIG. 26c

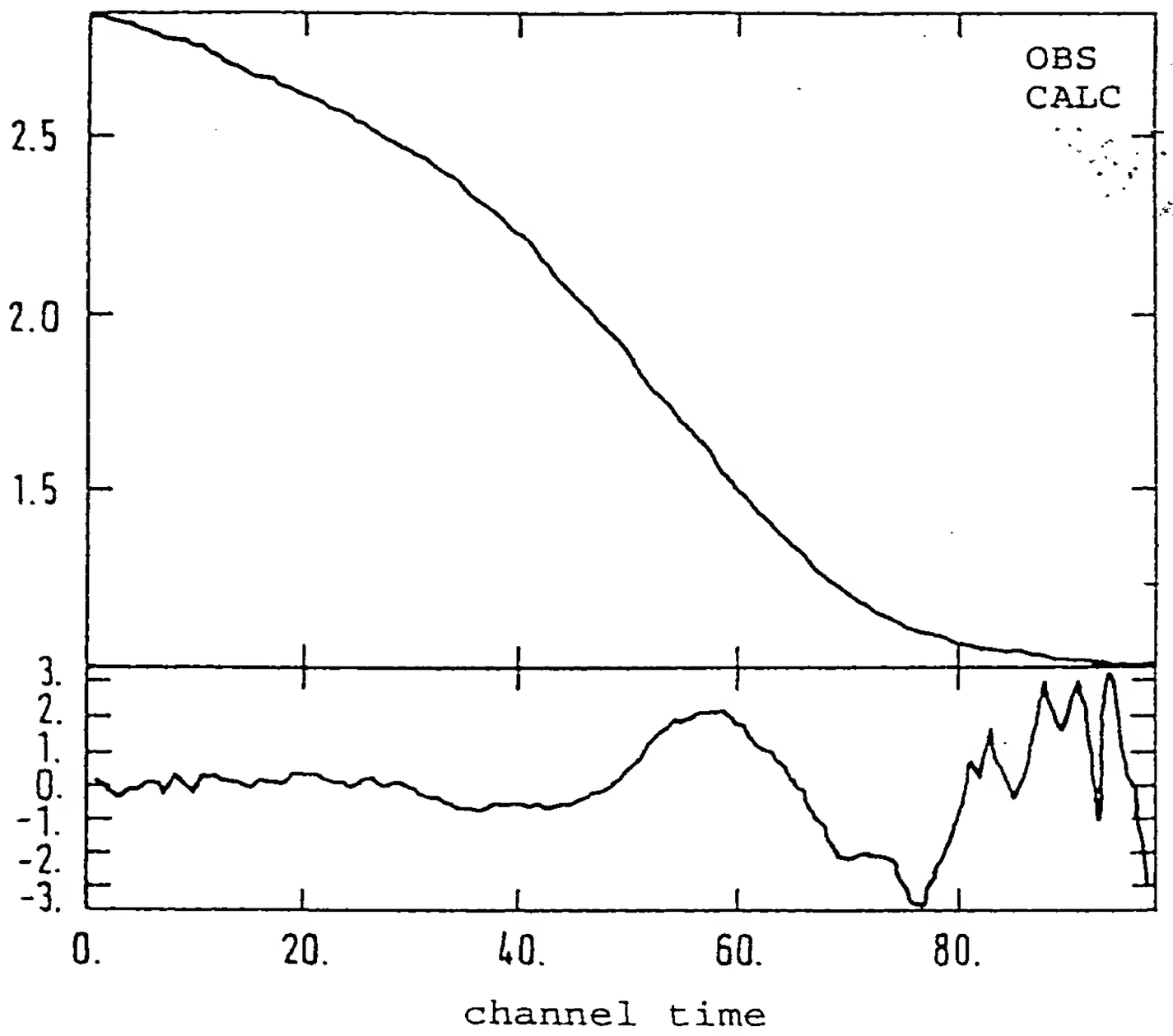


FIG. 27

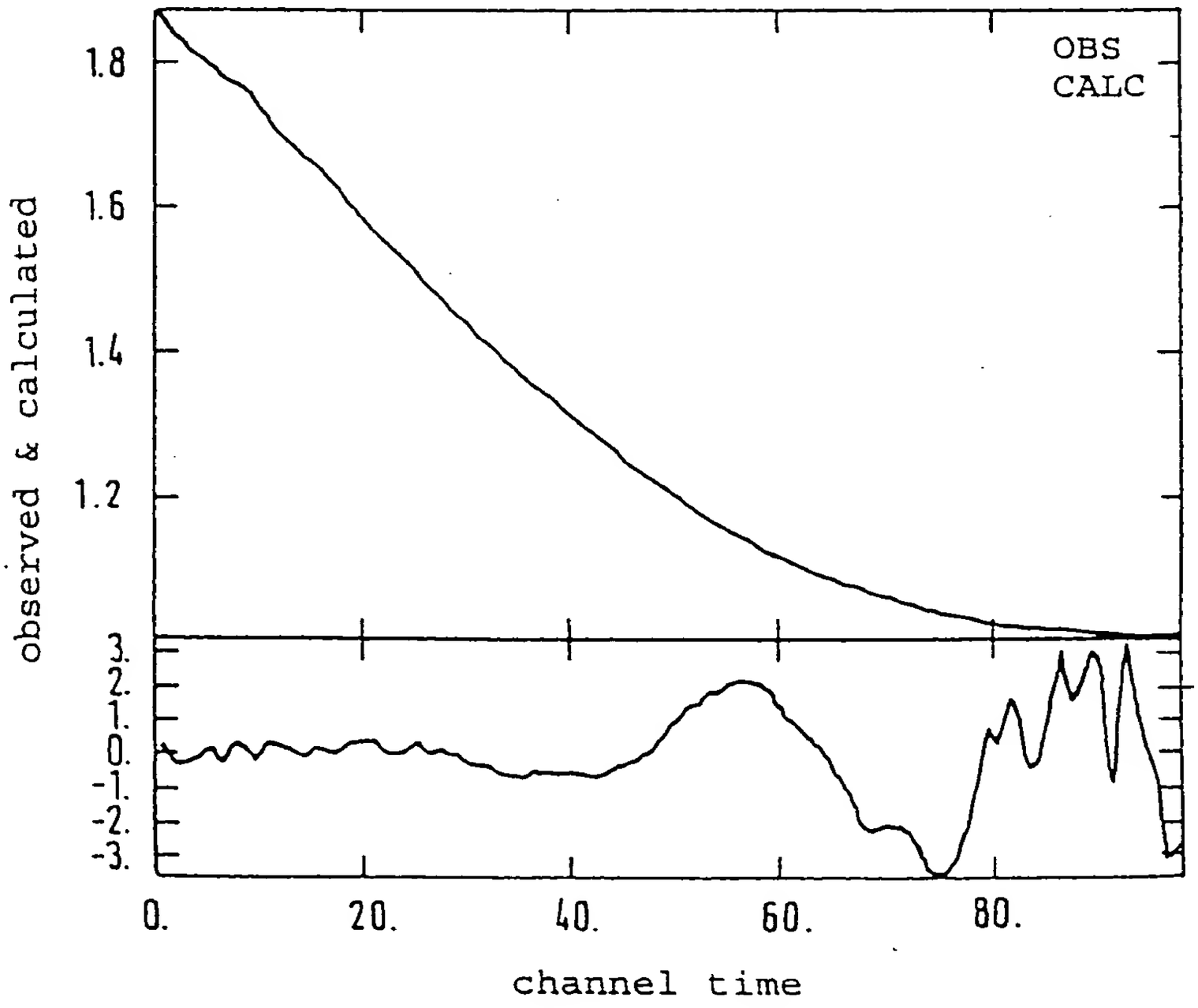


FIG. 28a

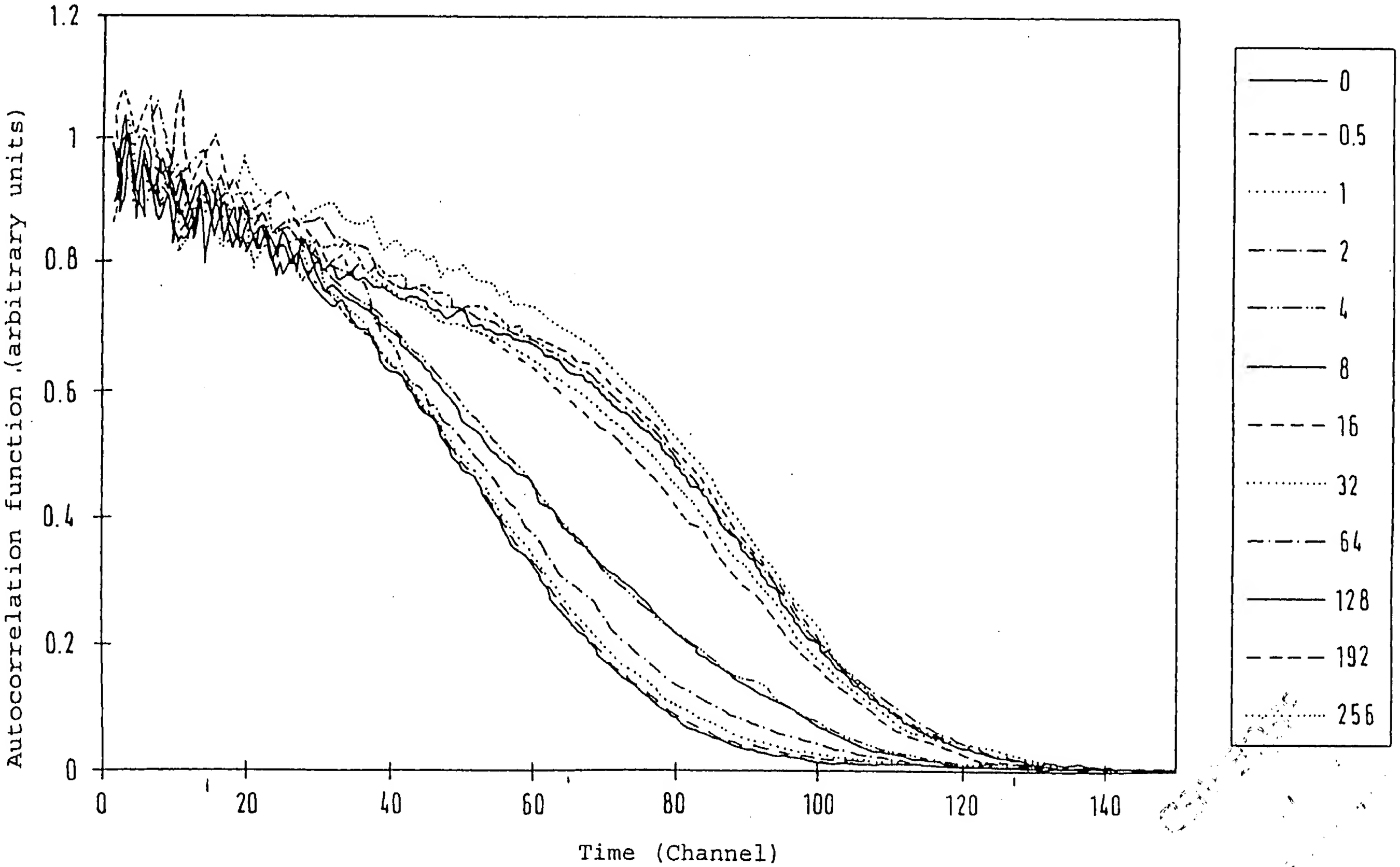

Autocorrelation function (arbitrary units)
1.2
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
140
Time (Channel)
0
0.5
1
2
4
8
16
32
64
128
192
256

FIG. 28b

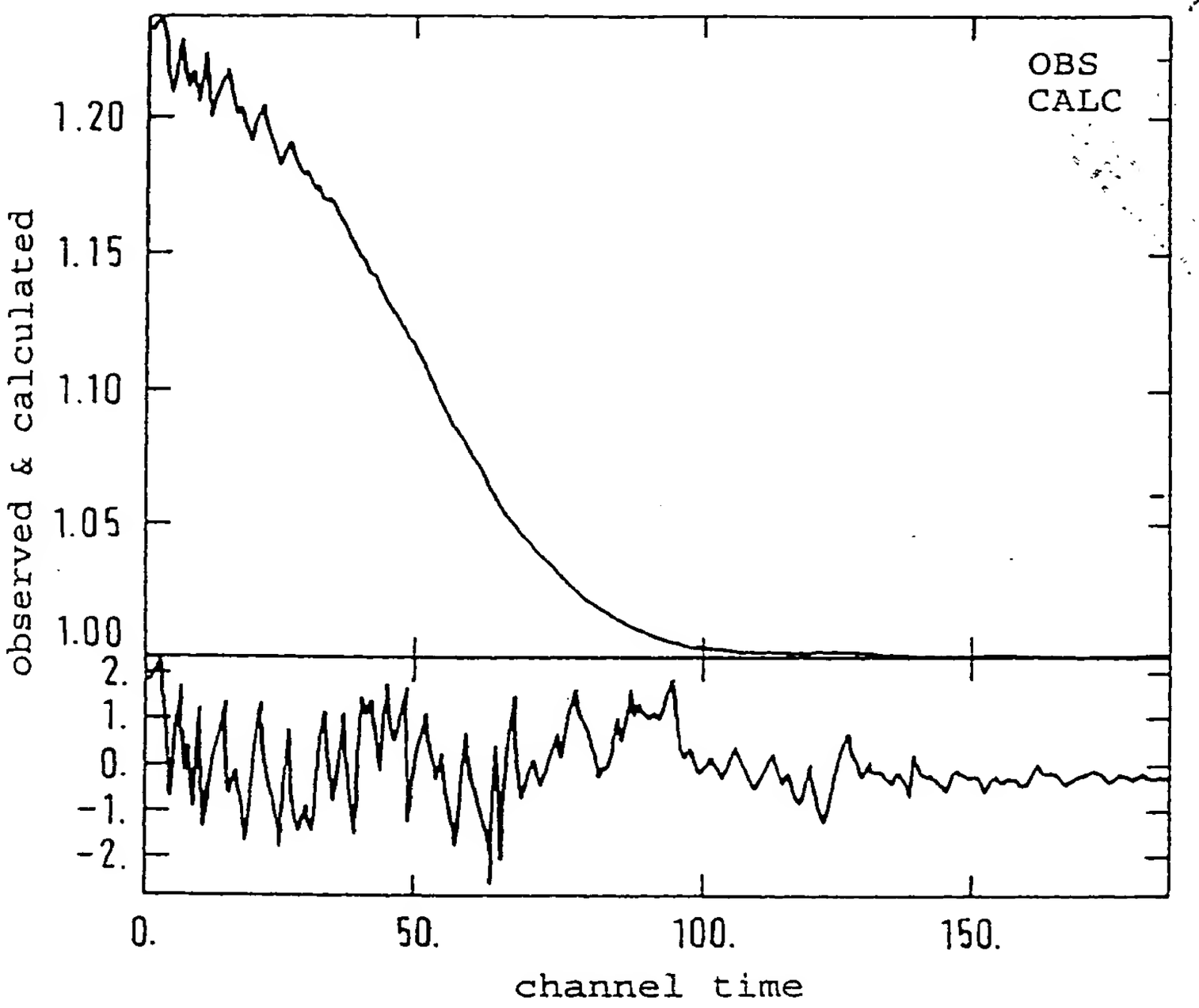


FIG. 28c

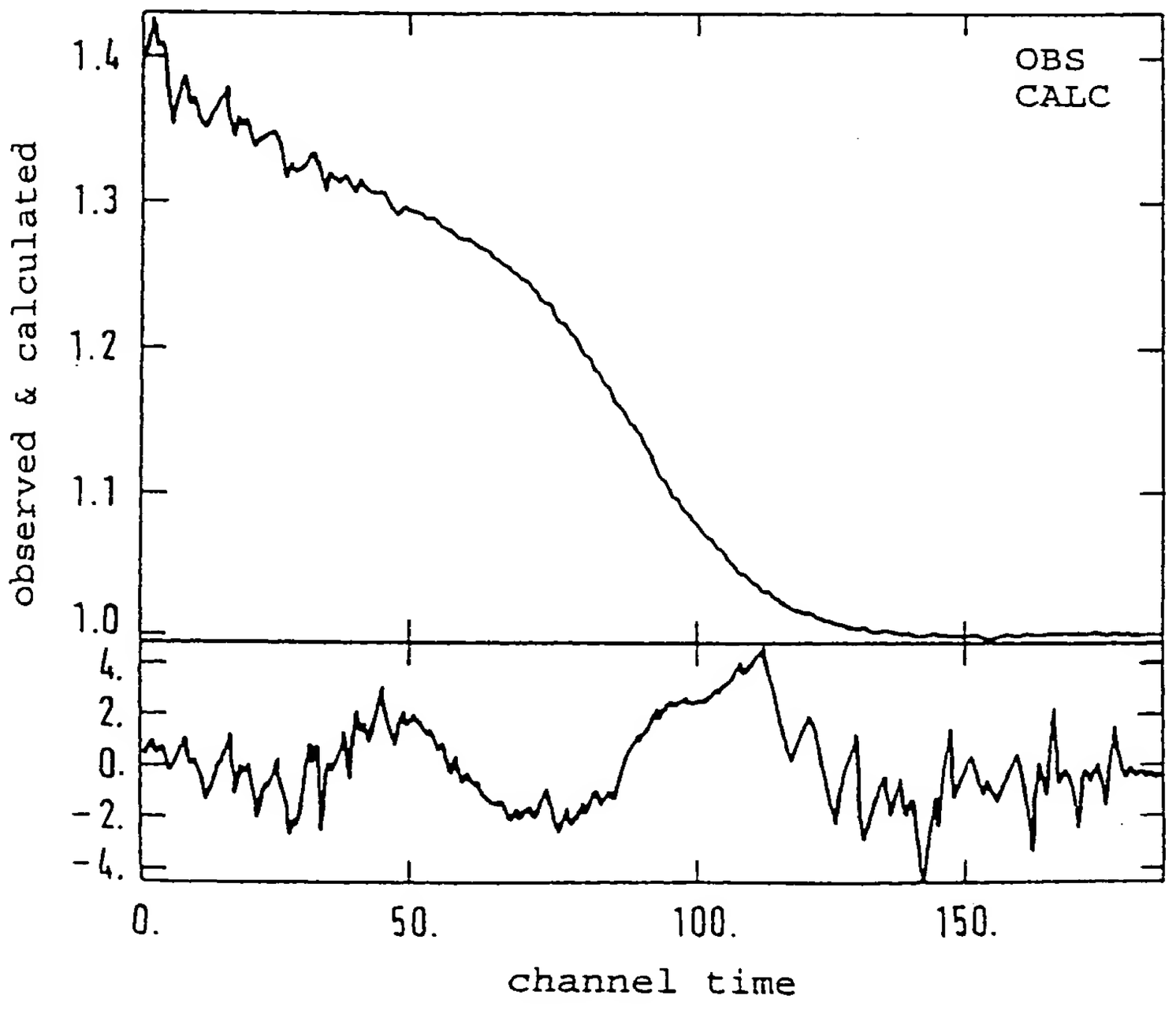


FIG. 29

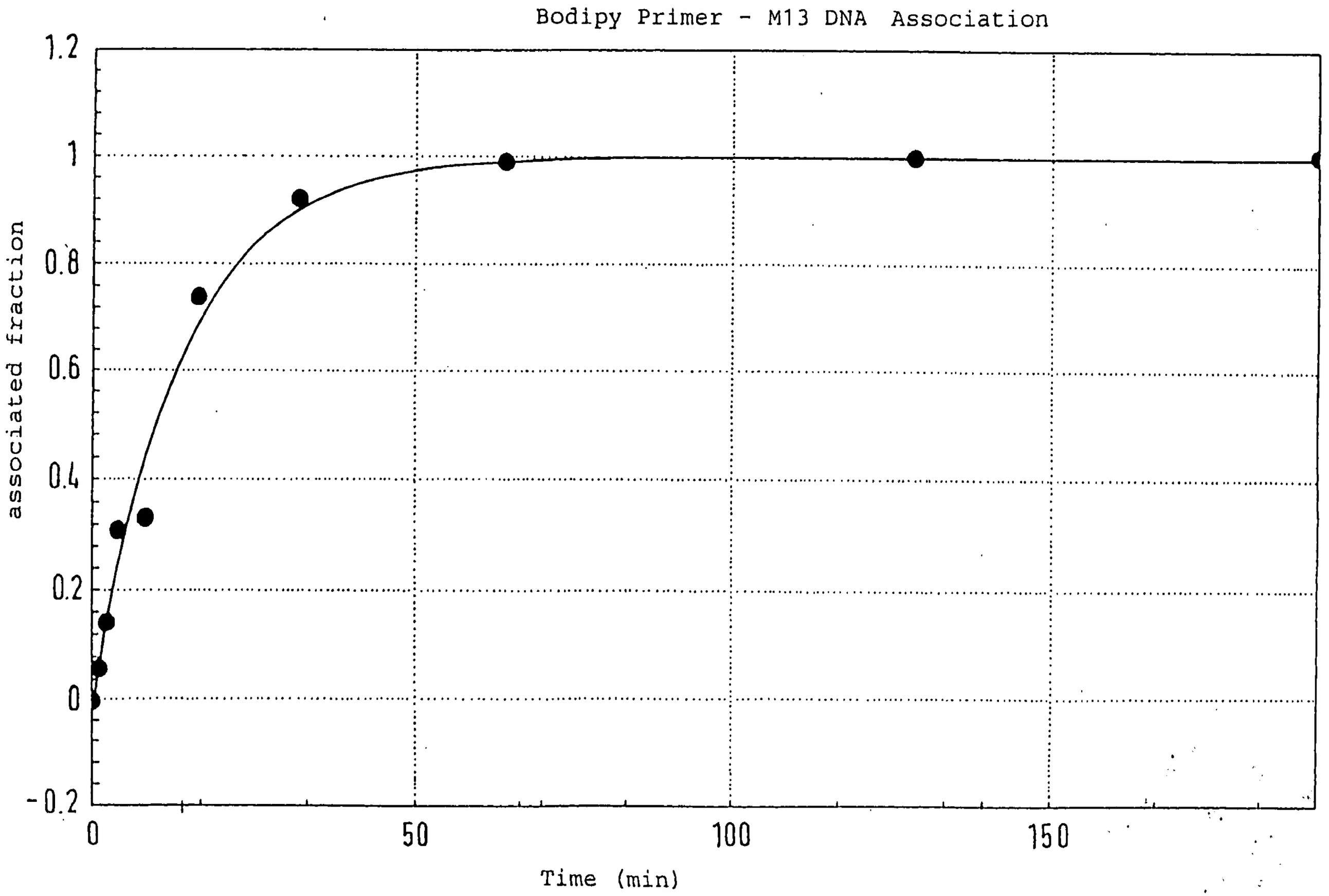

Bodipy Primer - M13 DNA Association
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
associated fraction
0
50
100
150
Time (min)

FIG. 30

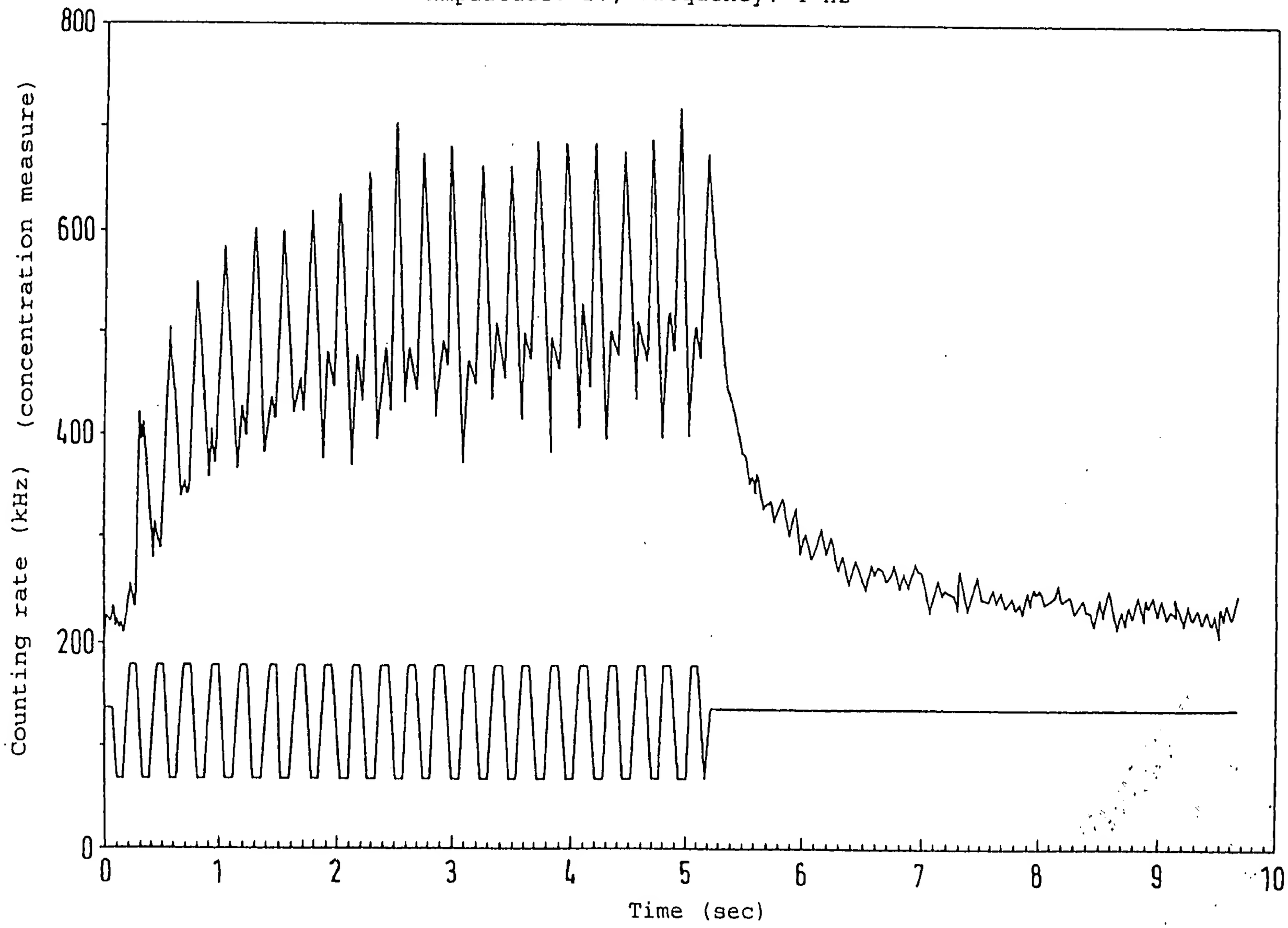

RDV10.DAT (Rho-dUTP with steel tips)
Amplitude: 2V, Frequency: 4 Hz
Counting rate (kHz) (concentration measure)
800
600
400
200
0
0
1
2
3
4
5
6
7
8
9
10
Time (sec)

FIG. 31a

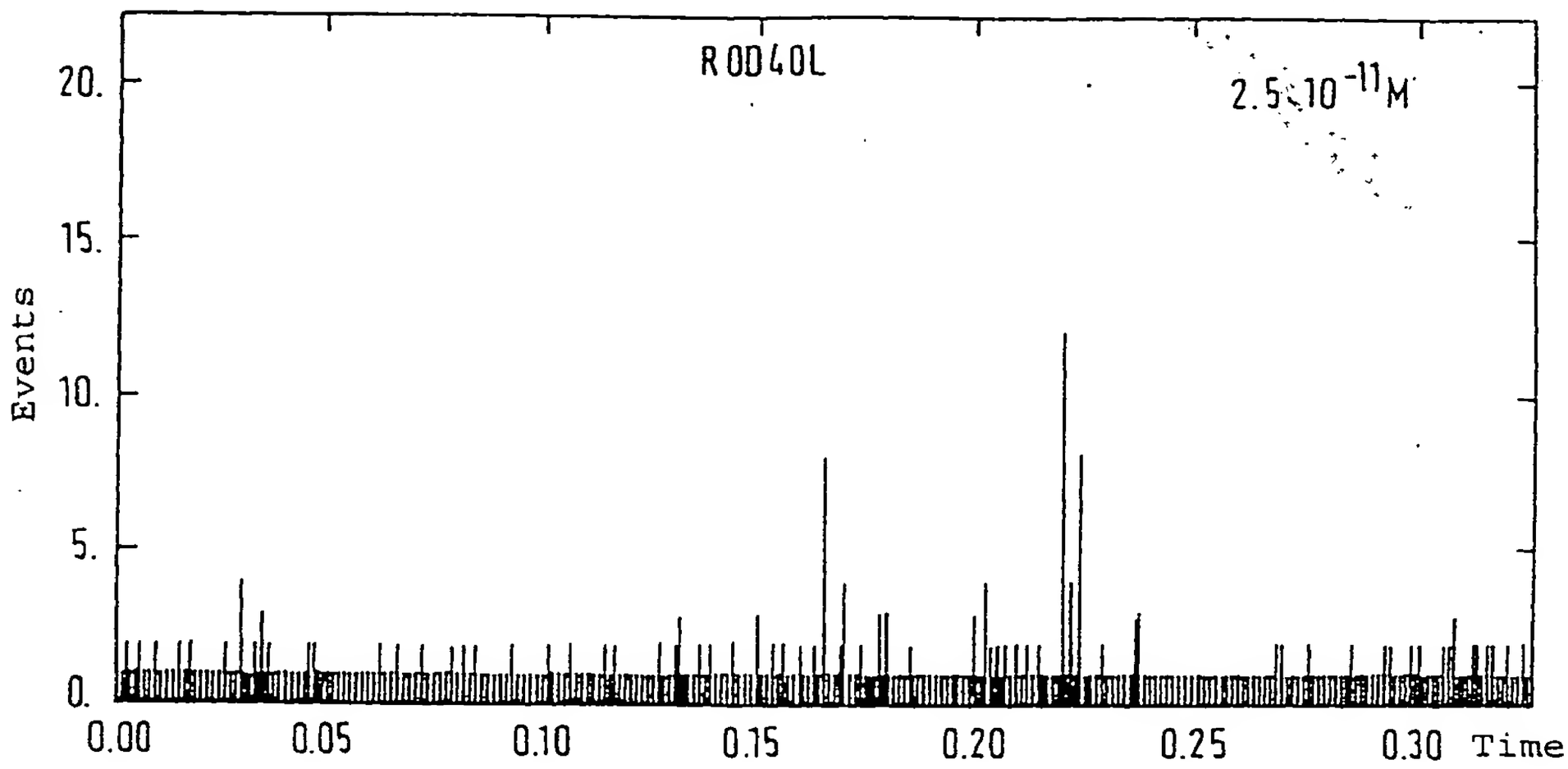


FIG. 31b